

[FOREWORD](#)

[INTRODUCTION](#)

3,5,5'-TRIMETHYL-1-HEXANOL
CAS N°: 3452-97-9

SIDS Initial Assessment Report
for
SIAM 14
(Paris, 26-28th March 2002)

Chemical Name: 3,5,5-Trimethyl-1-hexanol

CAS No: 3452-97-9

Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:

Mr. Yasuhisa Kawamura
Ministry of Foreign Affairs, Economic Affairs Bureau, Second International
Organizations Division.

Industry:

Mr. Hiroshige Maruyama,
KYOWA HAKKO KOGYO CO., LTD.
E-mail: hiroshige.maruyama@kyowa.co.jp

HISTORY: This substance was sponsored by Japan under the ICCA Initiative and was submitted for first discussion at SIAM 14.

PEER REVIEW PROCESS:

The industry collected new data and prepared the updated IUCLID, and draft versions of the SIAR and SIAP. Japanese government peer-reviewed the documents, audited selected studies.

TESTING:

No testing (X)
Testing ()

Deadline for circulation: 1/2/02

Date of circulation: 1/2/02

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	3452-97-9
Chemical Name	3,5,5-Trimethyl-1-hexanol
Structural Formula	$ \begin{array}{ccccccc} & & \text{CH}_3 & & \text{CH}_3 & & \\ & & & & & & \\ \text{H}_3\text{C} & - & \text{C} & - & \text{CH}_2 & - & \text{CH} & - & \text{CH}_2 & - & \text{CH}_2 & - & \text{OH} \\ & & & & & & & & & & & & \\ & & \text{CH}_3 & & & & & & & & & & \end{array} $

RECOMMENDATIONS

The chemical is currently of low priority for further work

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

There is no available information on toxicokinetics and metabolism of 3,5,5-trimethyl-1-hexanol. In an acute oral toxicity study [OECD TG 401] in rats, the LD₅₀ for this substance was more than 2000 mg/kg. In both a semi-occlusive patch test and an OECD 405 eye irritation assay 3,5,5-trimethyl-1-hexanol was a moderate irritant to both skin and eye. There is no information on sensitization.

In the OECD combined repeated dose and reproductive/ developmental toxicity screening test [OECD TG 422], this substance was administered by gavage (male rat 46 days, female rat from 14 days before mating to day 3 of lactation) at the dose levels of 12, 60 and 300 mg/kg/day.

Histopathological examination revealed a slight to moderate degree of hyaline droplet and eosinophilic body in proximal tubular epithelium in kidneys in all dosed male rats, which were confirmed as an accumulation of alpha-2u-globulin complex by immuno-staining. A slight to moderate degree of renal tubular epithelial regeneration and formation of granular casts in kidneys in males of the 60 and 300 mg/kg groups, a slight degree of irregularity in the shape of follicles, columnar change of the follicular epithelium and a decrease of colloid in the thyroid in males of the 300 mg/kg group were observed. In female rats, a slight degree of renal epithelial fatty change in the 60 and 300 mg/kg groups, and atrophy of the thymus in the 300 mg/kg group were observed. On the basis of these findings, the NOAEL of 3,5,5-trimethyl-1-hexanol for repeat dose toxicity was considered to be 12 mg/kg/day for males and females.

In the above OECD combined repeated dose and reproductive/ developmental toxicity screening test [OECD TG 422], a decrease in implantation rate was observed in the 60 and 300 mg/kg group. Total litter loss in two dams of the 300 mg/kg group was observed, and the number of pups born alive decreased in the 60 and 300 mg/kg groups. Because of the limitation of the methodology employed, it is not possible to distinguish if the cause was due to maternal toxicity or due to a direct effect on the fetus. With regard to effects on neonates, viability on day 4 of lactation decreased in the 300 mg/kg group, and male and female pups of the 300 mg/kg group showed lower body weights on day 0 of lactation.

On the basis of these findings, the NOAELs for reproductive/developmental toxicity were considered to be 12 mg/kg/day for parents and 12 mg/kg/day for the F1 generation, respectively.

The chemical showed negative results in bacterial mutation tests [OECD TG 471 & 472] and a chromosomal aberration test *in vitro* [OECD TG 473] with and without metabolic activation.

Environment

3,5,5-Trimethyl-1-hexanol is slightly soluble in water (450 mg/L at 25 °C). Log Pow and vapor pressure of this substance are 3.42 (at 25 °C) and 0.0901 hPa (at 25 °C), respectively. The half life for degradation in air is estimated to be 36 hr. In water, this substance is stable at pH 4,7 and 9 at 50°C.

If released into the aquatic environment from waste water, 3,5,5-trimethyl-1-hexanol would mostly remain in the water compartment. This substance is not readily biodegradable and has a low potential for bioaccumulation (BCF = 3.9-8.1).

This chemical has been tested in a limited number of aquatic species including algae, daphnids and fish. The 0-72 h-EC₅₀ (growth rate: [OECD TG 201]) for algae (*Selenastrum capricornutum*) is 33.3 mg/L and the NOEC is 6.60 mg/L (the NOEC for biomass is 2.9 mg/L).

For daphnids, the acute 48h-EC₅₀ (immobility: [OECD TG 202]) was 6.77 mg/L. The chronic toxicity results (reproduction: [OECD TG 211]) were reported as: 21d-LC₅₀ > 3.87 mg/L, 21d-EC₅₀ = 2.09 mg/L (reproduction) and 21d-NOEC = 1.46 mg/L (reproduction). The LC₅₀s for acute toxicity in fish (*Oryzias latipes* and *Carasius auratus*) were reported to be 27.7 mg/L [OECD TG 203](96 h) and 16 mg/L (24 h), respectively. Furthermore in a prolonged toxicity test with fish [OECD TG 204], behavior change was observed, most frequently on the 3rd day of exposure, at each concentration higher than 3.2 mg/L. EC₅₀ and NOEC values calculated based on the observation of the 3rd day were 3.20 and 1.28 mg/L, respectively.

Exposure

The production volume of this substance is approximately 1,300 t/y in Japan. This substance is produced in closed systems. The main use is an intermediate as a raw material for the synthesis of plasticizers (i.e. phthalate) and esters.

The fugacity model (Mackay level III) suggests that if released to air, water or soil, the majority of this substance would distribute into water and soil.

If released to water, this substance is not readily biodegraded (4% based on BOD during 28 day). The BCF of 3.9-8.1 suggests that the potential for bioaccumulation in aquatic organisms is low.

This substance is produced and used in closed system. Therefore, occupational exposure is limited to sampling and maintenance at the production facilities. Moreover, the exposure time is very short. A maximum exposure level is estimated in a production site of Japan. Workers are recommended to wear protective equipment (masks and gloves) during the work. Therefore occupational exposure through inhalation of its vapor or by dermal adsorption is assumed to be negligible.

The consumer would not be directly exposed to this chemical.

NATURE OF FURTHER WORK RECOMMENDED

This chemical is currently of low priority for further work, because this chemical is a closed system intermediate with a low exposure potential and workers are protected by proper equipment. It is not bioaccumulative in the environment, and no effect levels are greater than 1 mg/L.

FULL SIDS SUMMARY

CAS NO: 3452-97-9	SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL			
2.1 Melting Point		JIS K 0064	< - 30 °C (243 K)
2.2 Boiling Point		Other (unknown)	190 °C (at 1,013 hPa)
2.3 Density		JIS K 0061	0.828 g/cm ³ at 20 °C
2.4 Vapour Pressure		OECD TG 104	9.01 Pa at 25 °C
2.5 Partition Coefficient (Log Pow)		OECD TG 107	3.42 at 23 °C
2.6A. Water Solubility		OECD TG 105	450 mg/L at 25 °C
B. pH			5.9-6.1 at 25 °C
pKa			No Data
2.12 Oxidation: Reduction Potential			No Data
ENVIRONMENTAL FATE AND PATHWAY			
3.1.1 Photodegradation		calculated	In air T _{1/2} = 36 hr
3.1.2 Stability in Water		OECD TG 111	Stable at pH 4,7 and 9 at 50°C
3.2 Monitoring Data			No Data
3.3 Transport and Distribution		Calculated (Level III Fugacity Model)	(Release 100% to air) Air Water Soil Sediment 9.9% 6.2% 83.1% 0.8%
			(Release 100% to water) Air Water Soil Sediment 1.3% 77.6% 11.1% 9.9%
			(Release 100% to soil) Air Water Soil Sediment 0.0% 0.3% 99.6% 0.0%
3.5 Biodegradation		OECD TG 301C	No biodegradation observed
3.7 Bioaccumulation	Carp (<i>Cyprinus carpio</i>)	OECD TG 305C	BCF (6 weeks) = 3.9-8.1 (100 ug/L)
ECOTOXICOLOGY			
4.1 Acute/Prolonged Toxicity to Fish	<i>Oryzias latipes</i>	OECD TG 203	LC ₅₀ (96hr) = 27.7 mg/L
		OECD TG 204	LC ₅₀ (7 d) > 20 mg/L LC ₅₀ (14 d) > 20 mg/L EC ₅₀ (behavior) = 3.20 mg/L NOEC (behavior) = 1.28 mg/L
4.2 Acute Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	<i>Daphnia magna</i>	OECD TG 202	EC ₅₀ (48 hr) = 6.77 mg/L
4.3 Toxicity to Aquatic Plants e.g. Algae	<i>Selenastrum capricornutum</i> (ATCC22662)	OECD TG 201	EC ₅₀ (72 hr) = 33.3 mg/L NOEC(72 hr) = 6.60 mg/L
4.5.2 Chronic Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	<i>Daphnia magna</i>	OECD TG 202	EC ₅₀ (21 d) = 2.09 mg/L LC ₅₀ (21 d) > 3.87 mg/L NOEC (21 d) = 1.46 mg/L
4.6.1 Toxicity to Soil Dwelling Organisms			No Data
4.6.2 Toxicity to Terrestrial Plants			No Data
4.6.3 Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)			No Data

CAS NO: 3452-97-9		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD ₅₀ > 2,000 mg/kg (male) LD ₅₀ > 2,000 mg/kg (female)
5.1.2	Acute Inhalation Toxicity			No Data
5.1.3	Acute Dermal Toxicity			No Data
5.2.1	Skin Irritation	rabbit	Other (unknown)	Moderately Irritating PII = 2.08
5.2.2	Eye Irritation	rabbit	OECD TG 405	Moderately Irritating
5.3	Skin Sensitisation			No Data
5.4	Repeated Dose Toxicity	Rat	OECD TG 422	NOAEL = 12 mg/kg/day (male) NOAEL = 12 mg/kg/day (female)
5.5	Genetic Toxicity <i>In Vitro</i>			
A.	Bacterial Test (Gene mutation)	S.typhimurium, E. coli	Japanese TG and OECD TG 471 & 472	- (With metabolic activation) - (Without metabolic activation)
B.	Non-Bacterial <i>In Vitro</i> Test (Chromosomal aberrations)	CHL cells	Japanese TG and OECD TG 473	- (With metabolic activation) - (Without metabolic activation)
5.6	Genetic Toxicity <i>In Vivo</i>			No Data
5.7	Carcinogenicity			No Data
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOAEL Parental = 12 mg/kg/day NOAEL F1 Offspring = 12 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity			No Data
5.11	Experience with Human Exposure			No Data

JIS: Japanese Industrial Standard

SIDS INITIAL ASSESSMENT REPORT (SIAR)

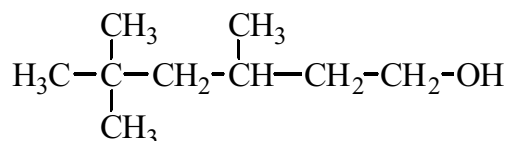
1. Identity

IUPAC name : 3,5,5-Trimethyl-1-hexanol

CAS number: 3452-97-9

Molecular formula: C₉H₂₀O

Structural formula:



Synonyms (Chemical Name):

1-Hexanol, 3,5,5-trimethyl- (TSCA, DSL, ENCS, AICS) (9CI)
 3,5,5-Trimethylhexan-1-ol (English, French, German) (DSL, EINECS)
 3,5,5-trimethylhexane-1-ol (French) (EINECS)
 3,5,5-Trimethyl hexanol (ECL)
 3,5,5-Trimethyl-1-hexanol
 3,5,5-Trimethylhexanol
 3,5,5-Trimethylhexyl alcohol
 i-Nonyl alcohol
 Nonylol
 TMH
 Alphao 920
 Nonanol
 Trimethylhexanol

Purity: = 90-94 % weight/weight
 Impurities: Octene, hydroformylation products (CAS-No 68527-05-9) 5-8 %
 isodecyl alcohol (CAS-No 25339-17-7) 1-3 %
 Additives: None

Physical and chemical properties:

ITEMS	PROTOCOL	RESULTS
Melting Point	JIS K 0064	< -30 °C
Boiling Point	Unknown	190 °C (at 1,013 hPa)
Density	JIS K 0061	0.828 g/cm ³ (at 20 °C)
Vapor Pressure	OECD TG 104	0.0901 hPa (at 25 °C)
	Unknown	41.3 hPa (at 100 °C)
Partition Coefficient (Log Pow)	OECD TG 107 (Flask shaking method)	3.42 (at 23 °C)
Water Solubility	OECD TG 105	450 mg/L (at 25 °C)
pH	Unknown	5.9-6.1 (at 25 °C, 450 mg/L)

JIS : Japanese Industrial Standard

Comments :

In the evaluation of chemical substances, it is important to use a substance whose structure can be clearly determined. 3,5,5-Trimethyl-1-hexanol is an alcohol of C-number 9. Many of the alcoholic products of C-number 9 are a mixture of isomers.

For most of the so-called 3,5,5-Trimethyl-1-hexanol products described in literature, the composition is not clear and even in the IUCLID data base, the data referred to are mostly those on other C-number 9 alcohols.

Therefore, in assessing 3,5,5-Trimethyl-1-hexanol, we had to adopt very recent, limited literature in which the composition is clearly given.

The alcoholic products of C-number 9 are shown in Appendix 3.

2. General Information on Exposure

- The production volume of this substance is approximately 1,300 t/y in Japan and 5000 t/y within the EU.
- This substance is produced in a closed system in Japan.
- This substance is predominately used as a raw material for the synthesis of plasticizers (i.e. phthalate) and esters.
- There are no sources of potential release to the environment except for sampling and maintenance at the production and use site.

2.1. Environmental Fate

- A generic fugacity model (Mackay level III) suggests that if released to air, water or soil, the majority of the substance would distribute into the compartment of soil and/or water as shown in Table 1.

Table 1: Environmental distribution of this substance using the fugacity model (Mackey level III) using three emission scenarios

	Release: 100% to air	Release: 100% to water	Release: 100% to soil
Air	9.9%	1.3%	0.0%
Water	6.2%	77.6%	0.3%
Soil	83.1%	11.1%	99.6%
Sediment	0.8%	9.9%	0.0%

- This substance is stable in water (no hydrolysis occurred over 5 days at 50 °C at pH 4,7, or 9).
- If released to water, this substance is not readily biodegraded (OECD301C: 4% based on BOD and COD and 55% based on GC during 28 day). The main degradation product is identified as being 3,5,5-trimethyl hexanoic acid [CITI, 1996]. The BCF = 3.9-8.1 suggests that the potential for bioaccumulation in aquatic organisms is low [CITI, 1998].
- The substance might be released from the facility through waste water. Based on the data of a Japanese company, the PEC (Predicted Environment Concentration) in the local surface water was calculated as 0.75×10^{-6} mg/L as shown in Appendix 1.
- If released into air, the vapor-phase of this substance will be degraded in the atmosphere by reaction with photochemically produced hydroxyl-radicals; the half time for this degradation reaction in air is estimated to be 36 hr.
- Degradation products: In general, aerobic biodegradation of alkylalcohols results in the oxidation of the alcohol group to a carboxylic acid group. This product is therefore expected to be transformed to 3,5,5-trimethylhexanoic acid.

2.2. Human Exposure

2.2.1. Occupational Exposure

- This substance is produced and used in closed systems. Therefore, occupational exposure is limited to sampling and maintenance at the production facilities. Moreover, the exposure time is very short. The major route of occupational exposure to this substance is inhalation and dermal.

- No information is available on the atmospheric concentration at the workplace.
- In Japan, this substance is produced at a single site in a “closed system” by a two-step process from octene involving 20 workers. Workers are required by the employer to wear appropriate protection implements at the workplace. Personal exposure is specified to occur during sampling for 1 min 5 times/day (number of samplers not specified). Safety equipment used are safety goggles, rubber gloves and protective uniform.
- A maximum exposure level is estimated as follows: If a certain worker (Body weight; 70 kg, respiratory volume; 1.25 m³/hour) is assigned to implement sampling operations for this substance, without protection, the maximum estimated human exposure (EHE) is calculated as 0.12 mg/kg/day in the worst case.
 - Sampling: 5 times/day, 1 min/time
 - Maintenance: 1 time/125day, 4 hr/time
 - Annual production day: 60 days
 - Vapor concentration: 524 mg/m³ (EASE model)

Workers wear protective gloves and goggles during the operation, so actual exposure in the workplace is considered to be lower than this EHE.

2.2.2. Consumer Exposure

The general use profile of this substance is as an intermediate in the production of esters (i.e. phthalates).

This substance is not directly used at all. Current consumer use has not been identified in Japan. Phthalates of this substance are mainly used as plasticizers of polyvinyl chloride (PVC) for cable overcoat and other esters are used as perfumes, flavor component etc.

2.2.3. Indirect Exposure via the Environment

Exposure via this route is unlikely. The chemical is not readily biodegradable, but it is not bioaccumulative. This substance is manufactured in “closed system” and waste-water from plants is treated by activated sludge before discharged to municipal drains. Other wastes are incinerated.

3. Human Health Hazards

3.1. Effects on Human Health

3.1.1. Toxicokinetics & Metabolism

There is no available information on toxicokinetics and metabolism of this substance.

3.1.2. Acute Toxicity

Available studies are shown in Table 2.

Table 2: Acute toxicity of 3,5,5-trimethyl-1-hexanol

Route	Animals	Values	Type	References
Oral (gavage)	Rat	>2000 mg/kg (male) >2000 mg/kg (female)	LD ₅₀	MHW, Japan (1997a)

The oral study [MHW, Japan (1997a)] was well conducted and described in detail. Therefore it was identified as a key study.

In this study, this substance was studied for oral toxicity in rats in a single dose toxicity test at 500, 1000, and 2000 mg/kg in both sexes. No deaths occurred of either males or females and the LD₅₀ was estimated to be more than 2000 mg/kg. A decrease in spontaneous motor activity was observed on the day of administration, and body weight gains were suppressed or tended to be suppressed from days 1 to 14 after administration in males and females. No changes were detected on autopsy or histopathological examination.

Dermal and inhalation studies on 3,5,5-trimethyl-1-hexanol are not available.

There is no available information on humans.

Conclusions:

Body weight gains were suppressed or tended to be suppressed from days 1 to 14 after administration in males and females in the 2000mg/kg group, but no changes were detected on autopsy or histopathological examination.

Oral LD₅₀: Male, > 2000 mg/kg; female, > 2000 mg/kg

3.1.3. Repeated Dose Toxicity

Available studies are shown in Table 3.

Table 3: Repeated Dose Toxicity of 3,5,5-trimethyl-1-hexanol

Route	Animals	Values	Type	References
Oral (gavage)	Rat	12 mg/kg (male) 12 mg/kg (female)	NOAEL	MHW, Japan (1997b)

Three further studies using unspecified 3,5,5-trimethyl-1-hexanol (nonanol rich in trimethylhexanol) are available but have not been used in this assessment.

The oral study [MHW, Japan (1997b)] was well conducted and described in detail. And this is the only available study specifically performed with 3,5,5-trimethyl-1-hexanol. Therefore it was identified as a key study.

According to the OECD combined repeated dose and reproductive/developmental toxicity screening test guidelines [OECD TG 422], SD (Crj: CD) rats received a gavage dose of 0 (vehicle; olive oil), 12, 60 or 300 mg/kg/day. The dosing period for males was 46 days, and from 14 days before mating to day 3 of lactation for females.

In the 300 mg/kg group, one female died on day 21 of gestation, and three others had to be killed because of weakness from days 14 to 19 of gestation. In these animals, body weights and food consumption were decreased, and histopathological examination revealed periportal fatty change in the liver, renal epithelial fatty change and fatty changed in other lesions.

Food consumption was increased and body weights tended to be increased in males of the 300 mg/kg group, but the opposite was the case for females receiving the highest dose.

Urinalysis, hematological and biochemical examinations revealed increases in urine volume and water consumption and slight decreases in red blood cell counts, hematocrit, hemoglobin concentrations, BUN and chloride in males of the 300 mg/kg group.

Absolute liver weights were increased in males and females of the 300 mg/kg group, relative liver weights were increased in males and females of the 60 and 300 mg/kg groups, absolute and relative weights of the right and left kidneys were increased in males of the 60 and 300 mg/kg groups, and relative weights of the right and left kidneys were increased in females of the 300 mg/kg group. Autopsy revealed pale discoloration of the kidneys in males of the 60 and 300 mg/kg groups, swelling of the kidneys in males of the 300 mg/kg group, and yellowish white discoloration of the liver in females of the 300 mg/kg group.

Histopathological examination revealed a slight or moderate degree of hyaline droplet and eosinophilic body in proximal tubular epithelium in kidneys of all dosed male rats, but these findings were not observed in females (alpha₂-globulin nephropathy). A slight to moderate degree of renal tubular epithelial regeneration and formation of granular casts in kidneys in males of the 60 and 300 mg/kg groups, a slight degree of irregularity in the shape of follicles, columnar change of follicular epithelium and decrease in colloid in thyroid in males of the 300 mg/kg group were observed. In female rats, a slight degree of renal epithelial fatty change in the 60 and 300 mg/kg groups, and atrophy of thymus in the 300 mg/kg group were observed.

Alpha₂-globulin nephropathy appears to be sex- and species-specific. That is, it occurs in male rats but not in female rats or in mice, rabbit, guinea pigs or humans, because they do not produce alpha₂-globulin. These phenomena were confirmed as an accumulation of alpha₂-globulin complex by immuno-staining. [Hamamura et al., in preparation] Therefore, it is suggested that humans are not at risk because humans do not synthesize alpha₂-globulin.

On the basis of these findings, the NOAEL of 3,5,5-trimethylhexan-1-ol for repeated dose toxicity was considered to be 12 mg/kg/day for male and female rats.

There is no available information on human toxicity.

Conclusions:

In the OECD combined repeated dose and reproductive/developmental toxicity screening test [MHW, Japan (1999d)], in males of the 60 and 300 mg/kg groups, absolute and relative weights of the kidney were increased and a slight to moderate degree of renal tubular epithelial regeneration and formation of granular casts in the kidneys were revealed. In females of the 60 and 300 mg/kg

groups, absolute and relative weights of the liver were increased and a slight degree of renal epithelial fatty change was revealed.

The NOAEL for repeated dose toxicity study was considered to be 12 mg/kg/day for male and female rats.

3.1.4. Genotoxicity

A bacterial study and a non-bacterial *in vitro* study are available. The summary of these studies is shown in Table 4.

Table 4: Genotoxicity studies of 3,5,5-trimethyl-1-hexanol

Type of test	Test system	Dose	Result	Reference
Bacterial test				
Ames test (reverse mutation)	<i>S. typhimurium</i> (strains TA98, TA100,TA1535,TA153 7) <i>E. coli</i> WP2 <i>uvr</i> A OECD TG 471 & 472	Up to 500 ug/plate	Negative (+ & -MA*)	MHW, Japan (1997c)
Non-bacterial in vitro test				
Chromosomal aberration test	CHL/IU cells OECD TG 473	Up to 0.10 mg/mL	Negative (+ & - MA)	MHW, Japan (1997d)

*MA: metabolic activation

Bacterial test

A reverse gene mutation assay was conducted in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guidelines 471 and 472, using the pre-incubation method (MHW, Japan, 1997c). This study was well controlled and considered to be appropriate to be selected as a key study.

3,5,5-Trimethyl-1-hexanol was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 *uvr*A, with or without an exogenous metabolic activation system.

For *Salmonella typhimurium*, cytotoxicity was observed at 150 ug/plate (TA100, TA1537), 250 ug/plate (TA1535, TA98, WP2) without S9 mix, and at 150 ug/plate (TA100, TA1537), 250 ug/plate (TA1535, TA98), 500 ug/plate (WP2) with S9 mix.

Non-bacterial in vitro test

A chromosomal aberration test in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guideline 473 was conducted using cultured Chinese hamster lung (CHL/IU) cells (MHW, Japan, 1997d). This study was well controlled and considered to be appropriate to be selected as a key study.

No structural chromosomal aberrations nor polyploidy in CHL/IU cells were induced up to the high concentration of 0.10 mg/mL with continuous treatment, and with short-term treatment with and without an exogenous metabolic activation system. At a dose of 0.2 mg/ml, no chromosome analysis was performed because of severe cytotoxicity.

There were no available data on genotoxicity *in vivo*.

Conclusions:

This substance is not genotoxic with and without an exogenous metabolic activation system in bacterial and mammalian cells with and without metabolic activation.

3.1.5. Carcinogenicity

There is no available information.

3.1.6. Reproductive/developmental Toxicity

Available studies are shown in Table 5.

Table 5: Reproductive/developmental toxicity of 3,5,5-trimethyl-1-hexanol

Route	Species	Result	Toxicity	References
Oral (gavage)	Rat	(Reproductive toxicity) NOAEL Parental = 12 mg/kg/day	Decrease in implantation rate was observed in the 60 and 300 mg/kg groups.	MHW, Japan (1997b)
		(Developmental toxicity) NOAEL F1 Offspring = 12 mg/kg/day	Number of pups born alive decreased in the 60 and 300 mg/kg groups.	

Only one report was reviewed (MHW, Japan, 1997b). The study was conducted according to well-designed protocols, giving detailed information. Therefore this study is considered to be a key study.

In the OECD combined repeated dose and reproductive/ developmental toxicity screening test by gavage [OECD TG 422], this substance was given at 0 (vehicle; olive oil), 12, 60 and 300 mg/kg/day to male rats for 46 days, and to female rats from 14 days before mating to day 3 of lactation. The details of the results of this study are as follows:

(Reproductive toxicity)

Decrease in implantation rate was observed in the 60 and 300 mg/kg group.

(Developmental toxicity)

Total litter loss in two dams of the 300 mg/kg group was observed, and the number of pups born alive was decreased in the 60 and 300 mg/kg groups. With regard to effects on neonates, viability on day 4 of lactation was decreased in the 300 mg/kg group, and male and female pups of the 300 mg/kg group showed lower body weights on day 0 of lactation.

On the basis of these findings, NOAELs of 3,5,5-trimethyl-1-hexanol for reproductive/developmental toxicity were considered to be 12 mg/kg/day for parents and 12 mg/kg/day for the F1 generation, respectively.

There is no available information on humans.

Conclusions:

NOAELs of 3,5,5-trimethyl-1-hexanol for reproductive/developmental toxicity were considered to be 12 mg for parents and 12 mg/kg/day for the F1 generation.

3.1.7. Others: Irritation; Sensitization; Corrosivity

Skin Irritation

Studies with rabbits using undiluted 3,5,5-trimethyl-1-hexanol found moderate irritation of the skin.

Table 6: Skin Irritation of 3,5,5-trimethyl-1-hexanol

Test method	Test conditions	Result	Reference
Semi-occlusive patch	0.5 ml of undiluted Nonanol under a semi-occlusive patch for 4 hours	Moderate Irritation; Mean scores for 24, 48, and 72 hours: Erythema = 1.83 Edema = 0.22 PII = 2.08	Exxon, 1992

Based on these findings, 3,5,5-trimethyl-1-hexanol is a moderate skin irritant.

Eye Irritation

Studies with rabbits using undiluted 3,5,5-trimethyl-1-hexanol found moderate irritation of the eye.

Table 7: Eye Irritation of 3,5,5-trimethyl-1-hexanol

Test method	Test conditions	Result	Reference
OECD 405	0.1 ml of undiluted Nonanol instilled into the conjunctival sac of the eye	Moderately Irritating	ExxonMobil, 2002

Based on these findings, 3,5,5-trimethyl-1-hexanol is a moderate eye irritant.

Sensitization

There is no available information on sensitization.

Conclusions:

Based on these findings, 3,5,5-trimethyl-1-hexanol is a moderate skin and eye irritant.

3.2. Initial Assessment of Human Health

There is no available information on toxicokinetics and metabolism of 3,5,5-trimethyl-1-hexanol.

In an acute toxicity study [OECD TG 401] with rats, the LD₅₀ of 3,5,5-trimethyl-1-hexanol was more than 2000 mg/kg.

Data on acute toxicity by other routes are not available. In a semi-occlusive patch test and OECD 405 eye irritation assay, 3,5,5-trimethyl-1-hexanol was a moderate irritant to both skin and eye. There is no information on sensitization.

Repeated dose toxicity data were obtained from the combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422] by gavage (male rats for 46 days, female rats from 14 days before mating to day 3 of lactation) at dose levels of 12, 60 and 300 mg/kg/day.

Histopathological examination revealed, a slight to moderate degree of hyaline droplet and eosinophilic body in proximal tubular epithelium in kidneys of all dosed male rats, which were confirmed as an accumulation of alpha₂-globulin complex by immuno-staining. A slight to moderate degree of renal tubular epithelial regeneration and formation of granular casts in kidneys in males of the 60 and 300 mg/kg groups, a slight degree of irregularity in the shape of follicles, columnar change of follicular epithelium and decrease in colloid in thyroid in males of the 300 mg/kg group were observed. In female rats, a slight degree of renal epithelial fatty change in the 60 and 300 mg/kg groups, and atrophy of the thymus in the 300 mg/kg group were observed.

On the basis of these findings, the NOAEL of 3,5,5-trimethyl-1-hexanol for repeat dose toxicity was considered to be 12 mg/kg/day for males and females.

As for the reproductive ability of parental animals, a decrease in implantation rate was observed in the 60 and 300 mg/kg group. Total litter loss in two dams of the 300 mg/kg group was observed, and the number of pups born alive decreased in the 60 and 300 mg/kg groups. With regard to effects on neonates, viability on day 4 of lactation decreased in the 300 mg/kg group, and male and female pups of the 300 mg/kg group showed lower body weights on day 0 of lactation.

On the basis of these findings, the NOAELs of 3,5,5-trimethyl-1-hexanol for reproductive/developmental toxicity were considered to be 12 mg/kg/day for parents and 12 mg/kg/day for the F1 generation.

The chemical showed negative results in a bacterial mutation test [OECD TG 471 & 472] and a chromosomal aberration test in vitro [OECD TG 473] with and without metabolic activation.

4. Hazards to the Environment

4.1. Aquatic Effects

This substance has been tested in a limited number of aquatic species. Results are summarized in Table 8.

Table 8: Aquatic toxicity of 3,5,5-trimethyl-1-hexanol

Organism	Test method	Result (mg/L)	Reference
<i>Aquatic plants</i>			
Green algae (<i>Selenastrum capricornutum</i>) ATCC 22662	OECD TG 201 72 hr (op,s)	EC ₅₀ (72 hr, gr) = 33.3 (mc) NOEC (72 hr, gr) = 6.6 (mc) EC ₅₀ (72 hr, bms) = 12.6 (mc) NOEC (72 hr, bms) = 2.95 (mc)	MOE, Japan (1997a)
<i>Invertebrates</i>			
Water flea <i>Daphnia magna</i>	OECD TG 202 24, 48 hr (op,ss)	EC ₅₀ (24 hr, imm) = 9.24 (mc) EC ₅₀ (48 hr, imm) = 6.77 (mc)	MOE, Japan (1997b)
	OECD TG 202 21 d (op, f)	LC ₅₀ (21 d) > 3.87 (mc) EC ₅₀ (21 d, rep) = 2.09 (mc) NOEC (21 d, rep) = 1.46 (mc)	MOE, Japan (1997c)
<i>Fish</i>			
Medaka (<i>Oryzias latipes</i>)	OECD TG 203 96 hr (op, ss)	LC ₅₀ (96 hr) = 27.7 (mc)	MOE, Japan (1997d)
	OECD TG 204 14 day (op, f)	LC ₀ (14 d) = 20 (nc) LC ₅₀ (14 d) > 20 (nc) EC ₅₀ (3rd d, behavior) = 3.20 (nc) NOEC (3rd d, rfa) = 1.28 (nc)	MOE, Japan (1997e)
<i>Carassius auratus</i>	Other:unknown	LC ₅₀ (24 h) = 16	Bridie et al. (1979)

Cl: closed system; *op*: open system; *f*: flow through; *s*: static; *ss*: semi-static; *nc*: nominal concentration (actual concentration not measured); *mc*: measured concentration; *gr*: growth rate; *bms*: biomass; *imm*: immobility; *rfa*: reduced feeding activity

Among the data shown here, an acute toxicity data for fish used unspecified 3,5,5-trimethyl-1-hexanol and was not described in detail. Other data were derived from experiments conducted under GLP, and the chemical concentrations in the testing media were monitored during the course of the experiments. Therefore, they were identified as key studies.

In the algae growth inhibition test [OECD TG 201], a 0-72h-EC₅₀ of 33.3 mg/L (*Selenastrum capricornutum*, growth rate was reported. The NOEC value determined was 6.60 mg/L. In the water flea test [OECD TG 202], the acute 48h-EC₅₀ value on immobility to *Daphnia magna* was 6.77 mg/L and in the chronic test with *Daphnia magna*, the 21d-LC₅₀ was greater than 3.87 mg/L and the 21d-EC₅₀ and the 21d-NOEC were 2.09 mg/L (reproduction) and 1.46 mg/L (reproduction), respectively. The LC₅₀s of acute toxicity in fishes (*Oryzias latipes* and *Carassius auratus*) were reported as 27.7 mg/L [OECD TG 203](96 h), and 16 mg/L (24 h), respectively. Furthermore in the prolonged toxicity test in fish [OECD TG 204], behavior changes were observed, most frequently on the 3rd day of exposure, at each concentration higher than 3.2 mg/L. At a concentration higher than 8 mg/L, all individuals showed abnormal behavior and reduced feeding activity throughout the

exposure, and at 3.20 mg/L these symptoms were observed only on the 3rd and 4th day in a few individuals. EC₅₀ and NOEC values calculated based on these observations of the 3rd day were 3.20 and 1.28 mg/L, respectively.

There is no available information on the toxicity to sediment dwelling organisms.

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

This substance could be released into aquatic environment from waste water, and would remain mostly in the water compartment. This substance is not readily biodegraded and has a low potential of bioaccumulation (BCF = 3.9-8.1).

This chemical has been tested in a limited number of aquatic species including algae, daphnids and fish. The 0-72 h-EC₅₀ (growth rate: [OECD TG 201]) for algae (*Selenastrum capricornutum*) is 33.3 mg/L and the NOEC is 6.60 mg/L (the NOEC for biomass is 2.9 mg/L). For daphnids, the acute 48h-EC₅₀ (immobility: [OECD TG 202]) was 6.77 mg/L. The chronic toxicity results (reproduction: [OECD TG 211]) were reported as: 21d-LC₅₀ > 3.87 mg/L, 21d-EC₅₀ = 2.09 mg/L (reproduction) and 21d-NOEC = 1.46 mg/L (reproduction). The LC₅₀s for acute toxicity in fish (*Oryzias latipes* and *Carasius auratus*) were reported to be 27.7 mg/L [OECD TG 203](96 h) and 16 mg/L (24 h), respectively. Furthermore in a prolonged toxicity test with fish [OECD TG 204], behavior change was observed, most frequently on the 3rd day of exposure, at each concentration higher than 3.2 mg/L. EC₅₀ and NOEC values calculated based on the observation of the 3rd day were 3.20 and 1.28 mg/L, respectively.

A PNEC = 0.0292 mg/L for the aquatic organisms was calculated from the 21 d – NOEC (1.46 mg/L) for *Daphnia magna* using an assessment factor of 50, because two chronic data (*Daphnia magna* and *Algae*) were available.

5. Conclusions and Recommendation

5.1. Conclusions

Exposure (Physical/chemical property, production, use and distribution)

The appearance of this product is liquid, slightly soluble in water (450 mg/L at 25°C). The vapor pressure of this substance is very low (9.01 Pa at 25°C).

The production volume of this substance is approximately 1,300 t/y in Japan and 5000 t/y within the EU. This substance is produced in closed systems. The main use is an intermediate for the synthesis of plasticizers (i.e. phthalates) and esters.

The fugacity model (Mackay level III) suggests that if released to air, water or soil, the majority of this substance would distribute into water and soil.

If released to water, this substance is not readily biodegraded (4% based on BOD during 28 day). The BCF = (3.9-8.1) suggests that the potential for bioaccumulation in aquatic organisms is low.

The substance might be released from the facility through waste water. Based on the data of a Japanese company, PEC (Predicted Environment Concentration) in the local surface water was calculated as 0.75×10^{-6} mg/L.

This substance is produced and used in closed systems. Therefore, occupational exposure is limited to sampling and maintenance at the production facilities. Moreover, the exposure time is very short. A maximum exposure level is estimated in a production site of Japan. If a worker (Body weight; 70kg, respiratory volume; 1.25m³/hour) is assigned to implement the sampling of this substance without protection, the maximum estimated human exposure (EHE) is calculated as 0.12 mg/kg/day in the worst case. Workers are required by the employer to wear appropriate protection implements (mask and glove) during the work. Therefore occupational exposure through inhalation of its vapor or by dermal adsorption is assumed to be negligible.

Consumers would not be directly exposed to this chemical.

Environment

This substance could be released into the aquatic environment from waste water, and would remain mostly into the water compartment. This substance is not readily biodegraded and has a low potential for bioaccumulation (BCF = 3.9-8.1).

This chemical has been tested in a limited number of aquatic species including algae, daphnids and fish. The 0-72 h-EC₅₀ (growth rate: [OECD TG 201]) for algae (*Selenastrum capricornutum*) is 33.3 mg/L and the NOEC is 6.60 mg/L (the NOEC for biomass is 2.9 mg/L). For daphnids, the acute 48h-EC₅₀ (immobility: [OECD TG 202]) was 6.77 mg/L. The chronic toxicity results (reproduction: [OECD TG 211]) were reported as: 21d-LC₅₀ > 3.87 mg/L, 21d-EC₅₀ = 2.09 mg/L (reproduction) and 21d-NOEC = 1.46 mg/L (reproduction). The LC₅₀s for acute toxicity in fish (*Oryzias latipes* and *Carasius auratus*) were reported to be 27.7 mg/L [OECD TG 203](96 h) and 16 mg/L (24 h), respectively. Furthermore in a prolonged toxicity test with fish [OECD TG 204], behavior change was observed, most frequently on the 3rd day of exposure, at each concentration higher than 3.2 mg/L. EC₅₀ and NOEC values calculated based on the observation of the 3rd day were 3.20 and 1.28 mg/L, respectively.

A PNEC = 0.0292 mg/L for the aquatic organisms was calculated from the 21 d – NOEC (1.46 mg/L) for *Daphnia magna* using an assessment factor of 50, because two chronic data (*Daphnia magna* and *Algae*) were available.

Human Health

There is no available information on toxicokinetics and metabolism of 3,5,5-trimethyl-1-hexanol. In an acute oral toxicity study [OECD TG 401] for rats, the LD₅₀ of this substance was more than 2000 mg/kg. In a semi-occlusive patch test and OECD 405 eye irritation assay, 3,5,5-trimethyl-1-hexanol was a moderate irritant to both skin and eye. There is no information on sensitization.

In the OECD combined repeated dose and reproductive/ developmental toxicity screening test [OECD TG 422], this substance was given by gavage (male rat 46 day, female rat from 14 days before mating to day 3 of lactation) at dose levels of 12, 60 and 300 mg/kg/day.

Histopathological examination revealed a slight to moderate degree of hyaline droplet and eosinophilic body in proximal tubular epithelium in kidneys of all dosed male rats, which were confirmed as an accumulation of alpha_{2u}-globulin complex by immuno-staining. A slight to moderate degree of renal tubular epithelial regeneration and formation of granular casts in kidneys in males of the 60 and 300 mg/kg groups, a slight degree of irregularity in the shape of follicles, columnar change of follicular epithelium and decrease in colloid in thyroid in males of the 300 mg/kg group were observed. In female rats, a slight degree of renal epithelial fatty change in the 60 and 300 mg/kg groups, and atrophy of the thymus in the 300 mg/kg group were observed.

On the basis of these findings, the NOAEL of 3,5,5-trimethyl-1-hexanol for repeat dose toxicity was considered to be 12 mg/kg/day for males and females.

In the above OECD combined repeated dose and reproductive/ developmental toxicity screening test [OECD TG 422], a decrease in implantation rate was observed in the 60 and 300 mg/kg groups. Total litter loss in two dams of the 300 mg/kg group was observed, and the number of pups born alive decreased in the 60 and 300 mg/kg groups. With regard to effects on neonates, viability on day 4 of lactation decreased in the 300 mg/kg group, and male and female pups of the 300 mg/kg group showed lower body weights on day 0 of lactation.

On the basis of these findings, the NOAELs of 3,5,5-trimethyl-1-hexanol for reproductive/ developmental toxicity were considered to be 12 mg/kg/day for parents, and 12 mg/kg/day for the F1 generation, respectively.

The chemical showed negative results in bacterial mutation test [OECD TG 471 & 472] and chromosomal aberration test in vitro [OECD TG 473] with and without metabolic activation.

5.2. Recommendations

The chemical is currently of low priority for further work.

6. References

- (2) Bridie et. al. (1979).The acute toxicity of some petrochemicals to goldfish. *Water Res.* 13(7), 623-626.
- (3) Chemical Inspection and Testing Institute, Japan, Report No. 81258K
- (4) Chemicals Evaluation and Research Institute(CERI), Japan (2001),unpublished data.
- (5) Chemicals Inspection & Testing Institute, Japan (1996) Report No. 21258
- (6) Chemicals Inspection & Testing Institute, Japan (1997a) Test No. 91736 Ministry of Environment, Japan
- (7) Chemicals Inspection & Testing Institute, Japan (1997b) Test No. 91737, Ministry of Environment, Japan
- (8) Chemicals Inspection & Testing Institute, Japan (1997c) Test No. 91738, Ministry of Environment, Japan
- (9) Chemicals Inspection & Testing Institute, Japan (1997d) Test No. 91739, Ministry of Environment, Japan
- (10) Chemicals Inspection & Testing Institute, Japan (1997e) Test No. 91740, Ministry of Environment, Japan
- (11) Chemicals Inspection & Testing Institute, Japan (1998) Report No. 51258
- (12) Chemicals Inspection & Testing Institute, Japan (2001) Report No. 81258III K
- (13) Chemicals Inspection & Testing Institute, Japan.(1997) Report No. 81258K
- (15) EBSI, 1992. Primary Dermal Irritation Study in the Rabbit
- (22) ExxonMobil Biomedical Sciences, 2002. Acute Eye Irritation Test
- (26) Material Safety Data Sheet, KYOWA HAKKO KOGYO CO., LTD. 2001
- (27) Ministry of Health and Welfare: Japan (1997a),Toxicity Testing Reports of Environmental Chemicals 5, 641-642
- (28) Ministry of Health and Welfare: Japan (1997b),Toxicity Testing Reports of Environmental Chemicals 5, 643-659
- (29) Ministry of Health and Welfare: Japan (1997c),Toxicity Testing Reports of Environmental Chemicals 5, 661-667
- (30) Ministry of Health and Welfare: Japan (1997d),Toxicity Testing Reports of Environmental Chemicals 5, 669-672

- (32) Rhodes et. al. (1984). The absence of testicular atrophy and in vivo and in vitro effects on hepatocyte morphology and peroxisomal enzyme activities in male rats following the administration of several alkanols. *Toxicol. Letts.* 21, 103-109.
- (33) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol. IIC, 3rd Revised Edition. Clayton and Clayton, eds. p.4626-4629.
- (34) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol. IIC, 3rd Revised Edition. Clayton and Clayton, eds. p. 4626-4629.
- (35) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol.IIC, 3rd Revised Edition. Clayton and Clayton, eds. p. 4626-4629.
- (37) U.S. EPA/OTS: Document #89-910000247. TSCA Section 8(e) submission.
- (40) CASARETT AND DOULL'S TOXICOLOGY: The Basic Science of Poisons Sixth Edition, p. 507-508
- (41) Hamamura et al., "Immunohistochemical analysis of hyaline droplet in male rat kidneys and the evaluation with regard to human health" in preparation.

Appendix 1: PEC in the local surface water estimated in Japan

$$\begin{aligned} \text{PEC}_{\text{local water}} &= 0.003 \text{ t/y} \times 0.1 / (0.4 \times 10^6 \text{ m}^3/\text{y} \times 1000) \\ &= 0.00075 \times 10^9 \text{ t/m}^3 = 0.75 \times 10^{-6} \text{ mg/L} \end{aligned}$$

Remarks: 1300 t/y production volume of TMH in Japan
 0.003 t/y emission to waste water (default, ≥ 1000 tone/year)
 0.1 WWTP factor
 300 d/y annual production days (default, < 25000 tone/year)
 $0.4 \times 10^6 \text{ m}^3/\text{y}$ flow rate per day of waste water in the treatment plant
 1000 dilution factor (sea)

Appendix 2: EHE for worker (worst case)

$$\begin{aligned} \text{EHE}_{\text{inh}} &= 524 \times 1.25 \times 0.08 / 70 \times 60/365 \\ &= 0.12 \text{ mg/kg/day} \end{aligned}$$

Cair 524 mg/m^3 (EASE model, estimate from vapour pressure)
 V 1.25 m^3/h (default)
 W 70 kg (default)
 t 0.08 h/day
 T (annual production day) 60 d

* sampling 1 min/time, 5 times/day = 0.08 h/d

Appendix 3: Alcoholic Products of C-number 9

	CAS Number	Chemical name	Synonyms
1	3452-97-9	3,5,5-trimethyl-1-hexanol	3,5,5-trimethylhexanol, i Nonylol alcohol, Nonylol 1-hexanol, 3,5,5-trimethyl, TMH, Alphanol 920, Nonanol, Trimethyl hexanol
2	68527-05-9	octene, hydroformylation products	ISONONYL ALCOHOL
3	68526-84-1	C8-C10-iso, C9-rich	Alphanol 900, alphanol 910, Exxal 9, INA, Isononanol, Isononyl alcohol
4	27458-94-2	Isononanol	Isononyl alcoho, Exxal 9, Exxol 9, Neoflex 9, C9DNB alcohol
5	28473-21-4	nonanol	
6	143-08-8	1-nonanol	1-hydroxynonane, n-Nonan-1-ol, Nonanol, Octyl carbinol, Pelargonic alcohol
7	68515-81-1	Nonanol, branched and linear	

SIDS DOSSIER

Existing Chemical : ID: 3452-97-9
CAS No. : 3452-97-9
EINECS Name : 3,5,5-trimethylhexan-1-ol
EINECS No. : 222-376-7
TSCA Name : 1-Hexanol, 3,5,5-trimethyl-
Molecular Formula : C₉H₂₀O

Producer Related Part

Company : KYOWA HAKKO KOGYO CO., LTD
Creation date : 24.06.2002

Substance Related Part

Company : KYOWA HAKKO KOGYO CO., LTD
Creation date : 24.06.2002

Memo : SIAM14

Printing date : 24.06.2002

Revision date :

Date of last Update : 24.06.2002

Number of Pages : 51

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. GENERAL INFORMATION

Id 3452-97-9
Date 24.06.2002

1.0.1 OECD and Company Information

Type : lead organisation
Name : KYOWA HAKKO KOGYO CO., LTD
Partner :
Date :
Street : 1-6-1, Othemachi, Chiyoda-ku
Town : 100-8185 Tokyo
Country : Japan
Phone : +81-3-3282-0057
Telefax : +81-3-3284-1801
Telex :
Cedex :
05.01.2002

Type :
Name : ICI Chemicals & Polymers Limited
Partner :
Date :
Street : PO Box 14, The Heath
Town : WA7 4QF Runcorn, Cheshire
Country : United Kingdom
Phone :
Telefax :
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
18.11.2001

Type :
Name : NOROXO
Partner :
Date :
Street : B.P. 19
Town : 62440 Harnes
Country : France
Phone :
Telefax :
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
05.01.2002

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

Name of recipient : Mr.Koji Tomita,Ministry of Foreign Affair,Economic Affaris Bureau, Second International Organisations Div.
Street : 2-2-1 Kasumigaseki, Chiyoda-ku
Town : 100 Tokyo
Country : Japan
Phone : +81-3-3581-0018
Telefax : +81-3-3581-9470
Telex :
Cedex :
05.01.2002

1. GENERAL INFORMATION

Id 3452-97-9
Date 24.06.2002

1.1 General Substance Information

Substance type : organic
Physical status : liquid
Purity : 90- 94 % w/w
Source : KYOWA HAKKO KOGYO Co., LTD.
05.01.2002

Substance type : organic
Physical status : liquid
Purity : % w/w
Source : EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
05.01.2002

1.1.0 Details on template

1.1.1 Spectra

Type of spectra : NMR
Type of spectra : UV
Type of spectra : IR
Type of spectra : mass spectrum
Type of spectra : GC

1.2 Synonyms

3,5,5-trimethyl-1-hexaneol
05.01.2002

3,5,5-trimethylhexane-1-ol
17.05.2001

3,5,5-trimethylhexanol
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
06.04.1994

3,5,5-Trimethylhexanol
17.05.2001

Alphanol 920
Source : ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
14.03.1994

i-Nonyl alcohol
18.09.2001

Nonanol
Source : NOROXO Harnes
ICI Chemicals & Polymers Limited Runcorn, Cheshire
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)

1. GENERAL INFORMATION

Id 3452-97-9
Date 24.06.2002

06.04.1994

Nonylol

17.05.2001

TMH

14.09.2001

Trimethylhexanol

Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)

06.04.1994

1.3 Impurities

CAS-No : 68527-05-9
EINECS-No : 271-250-8
EINECS-Name : Octene, hydroformylation products
Contents : 5 - 8 % w/w
Source : KYOWA HAKKO KOGYO Co., LTD.
Flag : Critical study for SIDS endpoint
 05.01.2002

CAS-No : 25339-17-7
EINECS-No : 246-869-1
EINECS-Name : isodecyl alcohol
Contents : 1 - 3 % w/w
Source : KYOWA HAKKO KOGYO Co., LTD.
Flag : Critical study for SIDS endpoint
 05.12.2001

1.4 Additives**1.5 Quantity**

Production during the last 12 months :
Import during the last 12 months :
Quantity produced : 1 000 - 5 000 tonnes in 2000
Remark : 1,300 t/y in Japan in 2000
 05.01.2002

1.6.1 Labelling

Labelling : no labelling required (no dangerous properties)
Nota :
Specific limits : no
R-Phrases :
S-Phrases :
 05.01.2002

1.6.2 Classification

1. GENERAL INFORMATION

Id 3452-97-9
Date 24.06.2002

Classification : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
05.01.2002

1.7 Use Pattern

Type : type
Category : Non dispersive use
05.01.2002

Type : type
Category : Use in closed system
16.05.2001

Type : industrial
Category : Chemical industry: used in synthesis
17.09.2001

1.7.1 Technology Production/Use**1.8 Occupational Exposure Limit Values**

Type of limit : other: None
Limit value :
05.01.2002

1.9 Source of Exposure

Memo : Potential human exposure: This substance is produced and used in closed system. therefore, occupational exposure is limited in the case of sampling and maintenance at the production facilities.
Moreover, the exposure time is very short. The major route of occupational exposure to this substance is inhalation and dermal.
At a production site: In Japan, at a single site in a "closed system" by two step process from octene involving 20 workers.
Produced Personal exposure is specified to occur during sampling for 1min 5 times/day (number of samplers not specified). Safety equipment used are safety goggles, rubbers gloves and protective uniform.
Industrial hygiene monitoring data are not available (Kyowa Yuka Co, Ltd, 2001).

1.10.1 Recommendations/Precautionary Measures**1.10.2 Emergency Measures****1.11 Packaging**

1. GENERAL INFORMATION

Id 3452-97-9
Date 24.06.2002

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. PHYSICO-CHEMICAL DATA

Id 3452-97-9
Date 24.06.2002

2.1 Melting Point

Value : <-70 °C
Sublimation :
Method : other:Not specified
Year :
GLP : no
Test substance : no data
Source : METI Japan
05.01.2002 (3)

Value : <-30 °C
Decomposition : no at °C
Sublimation : no
Method : other:no data
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Reliability : (2) valid with restrictions
Test procedure according to national standard (JIS K 0064)
Flag : Critical study for SIDS endpoint
05.01.2002 (26)

Value : <-60 °C
Sublimation :
Method : other: ASTM D97/87
Year : 1987
GLP : no data
Test substance :
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (16)

2.2 Boiling Point

Value : = 190 °C at 1013 hPa
Decomposition : no
Method : other
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
05.01.2002 (26)

2.3 Density

Type : density
Value : = .828 g/cm3 at 20° C
Method : other
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Reliability : (2) valid with restrictions
Test procedure according to national standard (JIS K 0061)

2. PHYSICO-CHEMICAL DATA

Id 3452-97-9
Date 24.06.2002

Flag : Critical study for SIDS endpoint
 05.01.2002 (26)

Type : density
Value : = .829 g/cm³ at 20° C
Method : other: not specified
Year :
GLP : no data
Test substance :
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
 18.11.2001 (17)

2.3.1 Granulometry

2.4 Vapour Pressure

Value : = .0901 hPa at 25° C
Decomposition : no
Method : OECD Guide-line 104 "Vapour Pressure Curve"
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Decomposition : no
Source : METI Japan
Test substance : Source:KYOWA HAKKO KOGYO CO., LTD. Lot No.304054
 Purity:90.4%
Reliability : (1) valid without restriction
 well conducted study, carried out by Chemicals Inspection &
 Testing Institute, Japan
Flag : Critical study for SIDS endpoint
 16.11.2001 (12)

Value : = 41.3 hPa at 100° C
Decomposition : no
Method : other (measured)
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Decomposition : no
Flag : Material Safety Dataset
 05.01.2002 (26)

Value : = 24 hPa at 100° C
Decomposition :
Method : other (calculated): not specified
Year :
GLP : no data
Test substance :
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
 18.11.2001 (17)

2.5 Partition Coefficient

Log pow : = 3.42 at 23° C

2. PHYSICO-CHEMICAL DATA

Id 3452-97-9

Date 24.06.2002

Method	OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"	
Year	: 1997	
GLP	: yes	
Test substance	: as prescribed by 1.1 - 1.4	
Result	: log Pow under three conditions:	
	Condition 1: run 1: 3.41 run 2: 3.38	
	Condition 2: run 1: 3.49 run 2: 3.38	
	Condition 3: run 1: 3.49 run 2: 3.39 average 3.42	
Source	: METI Japan	
Test substance	: 3,5,5-Trimethyl-1-hexanol TOKYO KASEI KOGYO CO.,LTD., Purity:93.8%	
Reliability	: (1) valid without restriction Well conducted study, carried out by Chemicals Inspection & Testing institute, Japan	
Flag	: Critical study for SIDS endpoint	(13)
05.01.2002		
Log pow	: ca. 3.1 - 3.5 at ° C	
Method	: other (calculated)	
Year	:	
GLP	: no data	
Test substance	:	
Source	: NOROXO Harnes EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)	
18.11.2001		(17)

2.6.1 Water Solubility

Value	: = 450 mg/L at 25 ° C	
Qualitative	: moderately soluble (100-1000 mg/L)	
Pka	: at 25 ° C	
PH	: = 5.9 - 6.1 at 450 mg/L and 25 ° C	
Method	: OECD Guide-line 105 "Water Solubility"	
Year	: 1997	
GLP	: no	
Test substance	: as prescribed by 1.1 - 1.4	
Source	: METI Japan	
Test substance	: 3,5,5-Trimethyl-1-hexanol TOKYO KASEI KOGYO CO.,LTD., Purity:93.8%	
Reliability	: (1) valid without restriction Well conducted study, carried out by Chemicals Inspection Testing Institute, Japan	
Flag	: Critical study for SIDS endpoint	(13)
05.01.2002		
Value	: < .1 other: wt% at 20 ° C	
Qualitative	:	
Pka	: at 25 ° C	
PH	: at and ° C	
Method	: other: not specified	
Year	:	
GLP	: no data	

2. PHYSICO-CHEMICAL DATA

Id 3452-97-9
Date 24.06.2002

Test substance :
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (17)

Value : = 486 mg/L at 25 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method :
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Result : 3,5,5-Trimethyl-1-hexanol
 MW 144.257g/mol
 Solubility in water(S)(ppm=parts per million)
 ppm @T(weight) 4.8611E+02
 ppm @T(mol) 6.0732E+01
 Henry's law constant(H)
 H@T (atm/mol frac) 4.2228E+00
 H@T (atm/mol m3) 7.6010E -05
Reliability : (4) not assignable
 05.01.2002 (39)

2.6.2 Surface Tension

2.7 Flash Point

Value : = 79 ° C
Type : closed cup
Method : other:no data
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Test procedure according to national standard (JIS)
Flag : Material Safety Dataset
 05.01.2002 (26)

Value : = 86 ° C
Type : other: not specified
Method : Directive 84/449/EEC, A.9 "Flash point"
Year : 1985
GLP : no data
Test substance :
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
 18.11.2001 (17)

2.8 Auto Flammability

Value : = 404 ° C at
Method : other
Year :
GLP : no
Test substance : no data
Flag : Material Safety Dataset
 05.01.2002 (26)

2. PHYSICO-CHEMICAL DATA

Id 3452-97-9
Date 24.06.2002

2.9 Flammability

Result : non flammable
Method : other: not specified
Year :
GLP : no data
Test substance :
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
02.06.1994

2.10 Explosive Properties**2.11 Oxidizing Properties****2.12 Additional Remarks**

3. ENVIRONMENTAL FATE AND PATHWAYS

Id 3452-97-9

Date 24.06.2002

3.1.1 Photodegradation

Type : air
Light source :
Light spect. : nm
Rel. intensity : based on Intensity of Sunlight
Conc. of subst. : at 25 degree C
Indirect photolysis
Sensitizer : OH
Conc. of sens. : 500000 molecule/cm3
Rate constant : = .00000000001059 cm3/(molecule*sec)
Degradation : 50 % after 36 hour(s)
Deg. Product :
Method :
Year : 2001
GLP : no
Test substance :
Method : Calculation by AOP Win v1.86(Syracuse Research Corporation)
Remark : The rate constant for gas-phase reaction between photochemically produced hydroxyl radicals and the test substance in atmosphere was calculated by AOP Win v1.86, which is based on the structure activity relationship methods developed by Dr. Roger Atkinson and co-workers. The half-life time of the substance was calculated with the daily average concentration of OH radical of 5E5 molecule/cm3 in atmosphere.
Test substance : 3,5,5-Trimethyl-1-hexanol(CAS 3452-97-9)
Conclusion : The half-life time of the substance by the reaction with photochemically produced OH radicals in air is 36 hours.
Flag : Critical study for SIDS endpoint
 05.01.2002 (4)

3.1.2 Stability in water

Type : abiotic
t1/2 pH4 : at degree C
t1/2 pH7 : at degree C
t1/2 pH9 : at degree C
Deg. Product :
Method : OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year : 1996
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : -Preliminary Test
 a)Water Temperature: 50 °C
 b)Nominal Concentration: ca. 200mg/L
 c)pH: pH4, pH7, pH9
 d)Number of Replicates: 2
 e)Test period: 5 days
Result : This chemicals is stable at PH 4,7,9.
 At the preliminary examination,it is cleared.
Source : METI Japan
Test substance : 3,5,5-Trimethyl-1-hexanol
 TOKYO KASEI KOGYO CO., LTD., Purity:9
Reliability : (1) valid without restriction
 Well conducted study,C arried out by Chemicals Inspection & Testing Institute,Japan
Flag : Critical study for SIDS endpoint
 05.01.2002 (13)

3. ENVIRONMENTAL FATE AND PATHWAYS

Id 3452-97-9
Date 24.06.2002

3.1.3 Stability in soil

3.2 Monitoring data

3.3.1 Transport between environmental compartments

Type : fugacity model level III
Media : other: air-water-soil-sediment
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method :
Year : 2001
Result : Estimated Distribution under three emission Scenarios

Compartment	release		
	100%to air	100%to water	100%to soil
air	9.9%	1.3%	0.0%
water	6.2%	77.6%	0.3%
soil	83.1%	11.1%	99.6%
sediment	0.8%	9.9%	0.0%

Attached doc. : Appendix:Parameters used in calculation of distribution by Mackay Level III fugacity model.
 3452979-Appendix.PDF

Conclusion : If this chemical is released into air, it is likely to be mainly distributed into soil compartment, and is released into water, likely to be distributed into other compartments.
 But if it is released into soil, it is unlikely to be distributed in to other compartments.

Flag : Critical study for SIDS endpoint
 05.01.2002

3.3.2 Distribution

3.4 Mode of degradation in actual use

3.5 Biodegradation

Type : aerobic
Inoculum : activated sludge
Concentration : 100mg/L related to Test substance
 related to
Contact time : 28 day
Degradation : 4 % after 28 day
Result : under test conditions no biodegradation observed
Control substance : Aniline
Kinetic : %
 %
Deg. Product : yes

3. ENVIRONMENTAL FATE AND PATHWAYS

Id 3452-97-9

Date 24.06.2002

Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year : 1996
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Deg. Product : 3302-10-1 221-975-0 3,5,5-trimethylhexanoic acid
Method : -Test Conditions:
a)Water Temperature: 24-26-C
b)Inoculum: standardized activated sludge, 30mg/L as suspended solid
c)Exposure Vessel Type: 300 mL culture bottle
d)Number of Replicate: 3
Result : Biodegradability of test substance
4% by BOD after 28days
4% by TOC after 28days
55% by GC after 28days
Source : METI Japan
Test substance : 3,5,5-Trimethyl-1-hexanol
TOKYO KASEI KOGYO CO., LTD., Purity:93.8%
Reliability : (1) valid without restriction
Well conducted study, carried out by Chemicals Inspection &
testing Institute, Japan
Flag : Critical study for SIDS endpoint
05.01.2002

(5)

3.6 BOD5, COD or BOD5/ COD ratio

BOD5
Method : other:AP HA(1971)No. 219
Year : 1979
GLP :
Concentration : related to
BOD5 : mgO₂/l
COD
Method : other:ASTM(1974) D 1252-67
Year : 1979
GLP :
COD : mg/g substance
Method : BOD: Tests were conducted in accordance with the standard dilution
method(APHA "Standard Methods" No.219 (1971)) a 20+-1 degree c for
period of 5days.
COD: Tests were conducted in accordance with the standard potassium
dichromate method described in ASTM D 1252-67 (reapproved 1974)
Result : The table below gives the results of our BOD and COD measurements,
expressed in grams of oxygen per gram of chemical. the results are also
related to the theoretical oxygen demand (ThOD) of each compound, the
amount of oxygen needed for complete oxidation to water and carbon
dioxide.
Alcohols

IUPAC name	ThOD g/g	BOD g/g	%ofThOD	COD g/g	%ofThOD
3,5,5-Trimethylalcohol	3.00	0.49	16%	2.80	93%

Reliability : (3) invalid
05.01.2002

(1)

BOD5
Method : other: APHA #507

3. ENVIRONMENTAL FATE AND PATHWAYS

Id 3452-97-9

Date 24.06.2002

Year : 1975
GLP : no data
Concentration : related to
BOD5 : = 220 mgO2/l
COD
Method : other: APHA #508
Year : 1975
GLP : no data
COD : = 860 mg/g substance
RATIO BOD5/ COD
BOD5/COD : = .256
 :
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
Test substance : The test substance was Exxal 9 (isononyl alcohol, CAS#
 68526-84-1).
 07.04.1994 (25)

3.7 Bioaccumulation

Species : *Cyprinus carpio* (Fish, fresh water)
Exposure period : 42 day at 25 degree C
Concentration : 100µg/l
BCF : 3.9 - 8.1
Elimination : no
Method : OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of
 Bioconcentration in Fish"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Result : BCF 3.9-8.1 at 100 ug/l
 4.0-6.3 at 10 ug/l
Source : METI Japan
Test substance : 3,5,5-trimethyl-1-hexanol
 TOKYO KASEI KOGYO CO., LTD., Purity: 92.3%
Reliability : (1) valid without restriction
 Well conducted study, carried out by Chemicals Inspection &
 Testing Institute, Japan
Flag : Critical study for SIDS endpoint
 05.01.2002 (11)

3.8 Additional remarks

4.1 Acute/prolonged toxicity to fish

Type : semistatic
Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/L
Analytical monitoring : yes
LC0 : m = 16.6
LC50 : m = 27.7
LC100 : m = 37.1
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : -Test Organisms:
a)Size (length and weight): length = 17-19 mm; weight = 0.063-0.11 g
b)Supplier/Sorce: obtained from commercial hatcheries -Test Condition:
a)Dilution Water Source: dechlorinated tap water
b)Dilution Water Chemistry: hardness = 55.6mg/L as CaCO₃, pH = 7.7, chlorine concentration <0.02 mg/L
c)Exposure Vessel Type: 2.5 L test solution in 3.0L glass vessel
d)Nominal Concentration(as mg/L): 7.9 - 40.0
(Nominal concentration << water solubility(450 mg/L))
e)Vehicle/Solvent and Concentrations: Vehicle;hydrogenated castor oil(HCO-40) 80.0mg/L, Solvent;Not used
f) Stock Solutions Preparations and Stability: Pipette or pour the appropriate amount of the solution (0.1wt% of test chemical with solubilizer hydrogenated caster oil HCO-40 2000 mg/L) into the test waters.
g)Number of Replicates: 2
h)Fish per Replicates: 5
i)Renewal Rate of Test Water: water renewal; 24 hrs
j)Water temperature 23-25 degree C (measured 24.0-24.3 degree C)
k)Intensity of Irradiation: room light
l)Photoperiod: 16h:8h light-dark cycle
-Test Parameter: mortality
-Analytical Method: gas chromatography
-Statistical Method:
a)Data Analysis: Not described
b)Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean,geometric mean, etc):timeweighted means

Result : Nominal concentrations:

Nominal concentration (mg/L)	Measured concentration(mg/L) (percentage of nominal)	0-hours	24-hours	Mean*
Control	n.d.	n.d.	n.d.	
Solvent Control	n.d.	n.d.	n.d.	
7.90	7.82 (99.0)	5.26 (66.6)	6.46 (81.8)	
11.9	11.2 (94.0)	7.74 (65.0)	9.36 (78.6)	
17.8	17.3 (97.2)	15.9 (89.4)	16.6 (93.3)	
26.7	24.9 (93.4)	23.4 (87.8)	24.2 (90.6)	
40.0	38.8 (96.9)	35.4 (88.6)	37.1 (92.7)	

Nominal concentration (mg/L)	Measured concentration(mg/L) (percentage of nominal)	0-hours	24-hours	Mean*
Control	n.d.	n.d.	n.d.	
Solvent Control	n.d.	n.d.	n.d.	
7.90	7.82 (99.0)	5.26 (66.6)	6.46 (81.8)	
11.9	11.2 (94.0)	7.74 (65.0)	9.36 (78.6)	
17.8	17.3 (97.2)	15.9 (89.4)	16.6 (93.3)	
26.7	24.9 (93.4)	23.4 (87.8)	24.2 (90.6)	
40.0	38.8 (96.9)	35.4 (88.6)	37.1 (92.7)	

* The values are expressed as timeweight calcaluated.

Nominal/measured concentration: 0hr;93.4-99.0 %,
24hr(water renewal);65.0-89.4%

-Water Temperature: 24.0-24.3 degree C

-Water Chemistry in test: PH 7.0-7.5; DO = 5.8-8.3
mg/L(Oxygen saturation level>=60%)

-Cumulative mortality:

Measured concentration (mg/L) Cumulative number of dead fish (Percent mortality)

	24-hr	48-hr	72-hr	96-hr
Control	0(0)	0(0)	0(0)	0(0)
Solvent control	0(0)	0(0)	0(0)	0(0)
6.46	0(0)	0(0)	0(0)	0(0)
9.36	0(0)	0(0)	0(0)	0(0)
16.6	0(0)	0(0)	0(0)	0(0)
24.2	1(10)	1(10)	1(10)	2(20)
37.1	10(100)	10(100)	10(100)	10(100)

-LC50 27.7 mg/L (95%confidence limits 16.6-37.1)

Statistical method : binomial

LC0 16.6mg/L

LC100 37.1mg/L

-Other effects : Toxic symptoms

Measured concentration (mg/L) Toxic symptoms
3-hour 24-hour 48-hour 72-hour 96-hour

	3-hour	24-hour	48-hour	72-hour	96-hour
Control	-	-	-	-	-
Solvent control	-	-	-	-	-
6.46	-	AB(10)	AB(10)	AB(10)	AB(8)
9.36	-	AB(10)	AB(10)	AB(10)	AB(10)
		LT(1)	LT(1)	LT(1)	
16.6	AB(6)	AB(10)	AB(10)	AB(10)	AB(10)
		LT(1)	LT(1)	LT(1)	
24.2	AB(5)	AB(9)	AB(9)	AB(9)	AB(6)
	IM(5)	LT(2)	LT(4)	LT(5)	LT(7)
			IM(2)		
37.1	-	n	n	n	n

The values in parentheses express the number of fish showing the symptom.

AB : Abnormal behavior

LT : Light body color

IM : Immobility

- : No symptom

n : No observation was made because all fish died at this observation time

Source : MOE Japan
Test substance : 3,5,5-trimethyl-1-hexanol
TOKYO KASEI KOGYO CO., LTD., Purity: 93.8%
Reliability : (1) valid without restriction
Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan

Flag : Critical study for SIDS endpoint (9)
09.12.2001

Type : flow through
Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 14 day
Unit : mg/L
Analytical monitoring : yes
NOEC : m = 1.28
LC0 : m = 20
LC50 : m > 20
EC50 (Behaviour) : m = 3.2
Method : OECD Guideline 204 "Fish, Prolonged Toxicity Test: 14-day Study"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method :
-Test Organisms:
a)Size (length and weight): length = 18-21 mm; weight = 0.082-0.14 g
b)Supplier/Source: obtained from commercial hatcheries-Test Condition:
a)Dilution Water Source: dechlorinated tap water
b)Dilution Water Chemistry: hardness = 55.6mg/L as CaCO₃, pH = 7.7, chlorine concentration <0.02 mg/L
c)Exposure Vessel Type: 1.8 L test solution in 3.0L glass vessel
d)Nominal Concentration(as mg/L): 0.512 - 20.0 (Nominal concentration << water solubility(450 mg/L))
e)Vehicle/Solvent and Concentrations: Vehicle;hydrogenated castor oil(HCO-40) 40.0mg/L, Solvent;Not used
f) Stock Solutions Preparations and Stability: The working solution (0.1wt% of test chemical with solbilizer HCO-40 controlled) was prepared with the dilution water. The test solution was supplied continuously by mixing the working solution and the dilution water with the help of a mechanically operated quantitative water-pump.
g)Number of Replicates: 1
h)Fish per Replicates: 10
i)Flow-through Rate : 25mL/min
j)Water temperature 23-25 degree C (measured 24.0-24.3 degree C)
k)Intensity of Irradiation: room light
l)Photoperiod: 16h:8h light-dark cycle

-Analytical Method: gas chromatography
-Statistical Method:
a)Data Analysis: Not described
b)Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean,geometric mean, etc):Not described

Result : -Nominal/measured Concentration:

Nominal concentration (mg/L)	Measured concentration(mg/L) (percentage of nominal)			
	0-day	7-day	14-day	Mean*
Control	n.d.	n.d.	n.d.	n.d.
Solvent Control	n.d.	n.d.	n.d.	n.d.
0.512	0.499 (97.6)	0.449 (87.7)	0.480 (93.8)	0.476 (93.0)
1.28	1.25 (97.6)	1.10 (85.7)	1.23 (96.2)	1.19 (93.1)
3.20	3.09 (96.6)	2.59 (80.8)	2.87 (89.8)	2.85 (89.1)
8.00	7.80	7.02	7.31	7.32

(97.5) (87.8) (91.4) (92.2)
20.0 17.6 16.7 17.1 17.1
(88.2) (83.6) (85.4) (85.7)

* Expressed as arithmetic means calculated
-Water Temperature: 23.9-24.3 degree C
-Water Chemistry in test: PH 6.9-7.5; DO = 7.6-8.3
mg/L(Oxygen saturation level>=60%)

-Cumulative mortality:

Nominal concentration (mg/L)	Cumulative number of dead fish mortality(%) vs time (day)													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Solvent control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.512	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.28	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3.20	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8.00	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20.0	0	0	0	0	0	0	0	0	0	1	1	1		

-LC50:

Exposure time 7days LC50 > 20mg/L
14days LC50 > 20mg/L

-Other effects : Toxic symptom

Nominal concentration (mg/L)	Toxic symptoms (day)						
	1-day	2-day	3-day	4-day	5-day	6-day	7-day
Control	-	-	-	-	-	-	-
Solvent control	-	-	-	-	-	-	-
0.512	-	-	-	-	-	-	-
1.28	-	-	-	-	-	-	-
3.20 AB	-	-	1	-	-	-	-
RFA		5	3				
8.00 AB	2	2	10	8	5	5	5
RFA	10	10	10	10	10	10	10
20.0 AB	10	10	10	10	10	10	10
RFA	10	10	10	10	10	10	10

(mg/L)	8-day	9-day	10-day	11-day	12-day	13-day	14-day
Control	-	-	-	-	-	-	-
Solvent control	-	-	-	-	-	-	-
0.512	-	-	-	-	-	-	-
1.28	-	-	-	-	-	-	-
3.20 AB	-	-	-	-	-	-	-
RFA	-	-	-	-	-	-	-
8.00 AB	5	5	5	4	2	-	-

RFA 10 10 10 10 10 10 10
20.0 AB 10 10 10 10 9 9 9
RFA 10 10 10 10 9 9 9
LT - - - 4 3 3 3

The values express the number of fish showing the symptom.

symptom
AB : Abnormal behavior
RFA: Reduced feeding activity
LT : Light body color
- : no symptom

-NOEC 1.28 mg/L
-EC50 3.20 (2.17-4.72) mg/L (Behavior)
Source : MOE Japan
Test substance : 3,5,5-Trimethyl-1-hexanol
TOKYO KASEI KOGYO CO., LTD., Purity:93.8%
Reliability : (1) valid without restriction
Well conducted study, carried out by Chemicals Inspection & Testing
Institute, Japan
Flag : Critical study for SIDS endpoint
09.12.2001 (10)

Type : other: not specified
Species : *Pimephales promelas* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/L
Analytical monitoring : no data
LC50 : = 5.7
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: 1-nonanol
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (38)

Type : static
Species : *Carassius auratus* (Fish, fresh water)
Exposure period : 24 hour(s)
Unit : µg/l
Analytical monitoring : yes
LC50 : = 16000
Method : other: not specified
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
11.12.2001 (2)

4.2 Acute toxicity to aquatic invertebrates

Type : semistatic
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit :

Analytical monitoring : yes
EC50 : m = 6.77
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : -Test Organisms:
a)Age at Study Initiation:<24 hours after hatching
b)Supplier/Source: Supplied from U.S. EPA Environmental Research Laboratory
-Test Condition:
a)Dilution Water Source: dechlorinated tap water
b)Dilution Water Chemistry: hardness = 55.6mg/L as CaCO₃, pH = 7.7, chlorine concentration <0.02 mg/L
c)Exposure Vessel Type: 300 ml Petri dish (diameter = 8.5 cm,depth = 5.7 cm)
d)Nominal Concentration(as mg/L): 4.94-25.0 (Nominal concentration << water solubility(450 mg/L))
e)Vehicle/Solvent and Concentrations: Vehicle;hydrogenated castor oil(HCO-40) 100.0mg/L, Solvent;Not used
f) Stock Solutions Preparations and Stability: Pipette or pour the appropriate amount of the solution (0.1wt% of test chemical with solubilizer hydrogenated castor oil HCO-40 4000 mg/L) into the testwaters.
g)Number of Replicates: 4
h)Individuals per Replicates: 5
i)Renewal Rate of Test Water: water renewal; 24 hrs
j)Water temperature: 19-21 degree C
k)Intensity of Irradiation: room light
l)Photoperiod: 16h:8h light-dark cycle
-Duration of the Test: 48hr
-Test Parameter: immobility
-Analytical Method: gas chromatography
-Statistical Method:
a)Data Analysis: Not described
b)Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean,geometric mean, etc):time-weighted means
Result : -Nominal/measured Concentration:

Nominal concentration (mg/L)	Measured concentration(mg/L)		
	0-hour	24-hour	Mean*
Control	n.d.	n.d.	n.d.
Solvent control	n.d.	n.d.	n.d.
4.94	5.29 (107)	3.54 (71.6)	4.35 (88.1)
7.41	8.0 (108)	5.41 (73.1)	6.63 (89.4)
11.1	11.7 (106)	8.16 (73.5)	9.83 (88.6)
16.7	16.7 (99.8)	13.3 (79.8)	14.9 (89.4)
25.0	23.7 (94.7)	20.0 (79.9)	21.8 (87.1)

* Expressed as timeweighted means calculated

-Water Temperature: 20.2-20.3 degree C
-Water Chemistry in test: PH 7.6-7.8; DO = 8.7-8.8 mg/L (Oxygen saturation level >=60%)

-Cumulative immobility:

Measured concentration (mg/L)	Cumulative number of Immobilized Daphnia (Percent immobility)	
	24-hour	48-hour
Control	0(0)	0(0)
Solvent control	0(0)	0(0)
4.35	0(0)	1(5)
6.63	3(15)	11(55)
9.83	14(70)	18(90)
14.9	18(90)	19(95)
21.8	19(95)	20(100)

-EiC50: 6.77 mg/L (48hr)

Exposure time (hour)	EiC50 (mg/L)	95%confidence limits (mg/L)
24	9.24	8.08 - 10.6
48	6.77	5.88 - 7.71

-NOECi: -

-LOECi(100% immobility): 21.8 mg/L (48hr)

Source : MOE Japan
Test substance : 3,5,5-Trimethyl-1-hexanol
 TOKYO KASEI KOGYO CO., LTD., Purity:93.8%
Reliability : (1) valid without restriction
 Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan
 Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan
Flag : Critical study for SIDS endpoint
 05.01.2002

(7)

4.3 Toxicity to aquatic plants e.g. algae

Species : *Selenastrum capricornutum* (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/L
Analytical monitoring : yes
NOEC : m = 6.60
EC50 : m = 33.3
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : -Test Organisms:
 a) Strain: ATC22662
 b) Supplier/Source: American Type Culture Collection
 c) Initial Cell Concentration: 1X10E+4
 -Test Condition:
 a) Test Medium: OECD medium
 b) Exposure Vessel Type: 100ml medium in a 500ml erlenmeyer flask with a silicon cap which allow ventilation (open)
 c) Nominal Concentration (as mg/L): 2.13-50.0

d) Stock Solutions Preparations and Stability: Test chemical was diluted to nominal concentration (solubilizer, HCO-40 100 mg/L) with OECD medium.
e) Number of Replicates: triplicate
f) Initial Cell Number: 10000 cells/ml
g) Water Temperature Range: 21-25 degree C (measured 23.2-20.8 degree C)
h) Light condition: 4400-4500 lux (continuous)
i) pH: 8.1 at start and 8.2-9.4 at end of the test
j) shaking: 100 rpm

-Test Parameter: cells/ml
-Analytical Method: gas chromatography
-Statistical Method:
a) Data Analysis: Not described
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc): time-weighted means
: -Nominal/measured Concentration:

Result

Nominal concentration (mg/L)	Measured concentration (mg/L) (percentage of nominal)		
	0-hour	24-hour	Mean*
Control	n.d.	n.d.	n.d.
Solvent control	n.d.	n.d.	n.d.
2.13	2.16 (102)	n.d. (0.923)	1.46 (68.4)
4.70	4.53 (96.3)	1.80 (38.2)	2.95 (62.8)
10.3	9.08 (88.2)	4.61 (44.8)	6.60 (64.1)
22.7	21.8 (96.2)	9.37 (41.3)	14.7 (64.9)
50.0	46.8 (93.5)	22.8 (45.5)	33.3 (66.7)

n.d.: <1.00 mg/L

* The value are expressed as time-weighted means calculated

-Water Temperature: 23.2-23.8 degree C
-Water Chemistry in test: PH 8.1 at start and 8.2-9.4 end of the test

-Effect Data/element values:
area method
EbC50(0-72hr) = 19.5 mg/L (95% c.i.: 14.8-25.8 mg/L)
12.6 mg/L (measured concentration)
NOEC = 4.70 mg/L
2.95 mg/L (measured concentration)
rate method
ErC50(24-48hr) = 49.9 mg/L (95% c.i.: none)
ErC50(24-72hr) > 50 mg/L (95% c.i.: none)
33.3 mg/L (measured concentration)
NOEC = 10.3 mg/L
6.60 mg/L (measured concentration)

-Cell density of *Selenastrum capricornutum* during exposure to 3,5,5-trimethyl-1-hexanol:

Nominal cell density (X10E+4 cells/ml)
concentration

(mg/L)	No.	0-hour	24-hour	48-hour	72hour
Control	1	1.0	3.1	22.6	96.0
	2	1.0	3.4	22.5	91.9
	3	1.0	2.9	20.2	83.3
Average		1.0	3.2	21.7	90.4
S.D.		0.0	0.2	1.3	6.5
Solvent control	1	1.0	3.0	21.8	103.2
	2	1.0	3.3	21.5	96.5
	3	1.0	3.3	21.4	85.8
Average		1.0	3.2	21.6	95.2
S.D.		0.0	0.1	0.2	8.8
2.13	1	1.0	3.4	21.1	89.8
	2	1.0	3.1	23.8	93.1
	3	1.0	3.1	20.7	99.1
Average		1.0	3.2	21.9	94.0
S.D.		0.0	0.1	1.7	4.7
4.70	1	1.0	3.2	21.3	86.0
	2	1.0	2.9	19.6	85.5
	3	1.0	3.4	20.4	99.7
Average		1.0	3.2	20.4	90.4
S.D.		0.0	0.2	0.8	8.1
10.3	1	1.0	2.5	14.8	66.2
	2	1.0	2.7	17.7	64.6
	3	1.0	2.5	16.7	66.2
Average		1.0	2.6	16.4	65.7
S.D.		0.0	0.1	1.5	0.9
22.7	1	1.0	2.4	10.0	48.1
	2	1.0	2.6	10.8	47.6
	3	1.0	2.3	10.9	42.3
Average		1.0	2.4	10.6	46.0
S.D.		0.0	0.2	0.5	3.2
50.0	1	1.0	1.5	4.2	11.6
	2	1.0	1.7	4.4	11.9
	3	1.0	1.8	4.1	11.2
Average		1.0	1.5	4.2	11.6
S.D.		0.0	0.2	0.1	0.3

-Growth inhibition of *Selenastrum capricornutum* during exposure to 3,5,5-trimethyl-1-hexanol:

Nominal concentration (mg/L)	Area No.	Inhibition (x10E+4) (0-72h)	Rate (%) (24-72h)	Inhibition (%)	
Control	1	1710	-	0.0712	-
	2	1660	-	0.0687	-

	3	1500	-	0.0696	-

	Average 1620		-	0.0698	-

Solvent control	1	1780	-9.41	0.0734	-5.11
	2	1690	-4.35	0.0750	-0.982
	3	1560	3.73	0.0680	2.68

	Average 1680		-3.34	0.0706	-1.14

2.13	1	1610	1.08	0.0685	1.93
	2	1700	-4.87	0.0709	-1.53
	3	1700	-4.77	0.0721	-3.27

	Average 1670		-2.85	0.0705	-0.957

4.70	1	1560	3.87	0.0683	2.20
	2	1510	7.13	0.0704	-0.854
	3	1710	-5.16	0.0706	-1.03

	Average 1590		1.95	0.0698	0.105

10.3	1	1150	29.2	0.0682	2.23
	2	1210	25.7	0.0661	5.35
	3	1200	26.3	0.0679	2.81

	Average 1180		27.1	0.0674	3.50

22.7	1	814	49.9	0.0628	10.0
	2	833	48.6	0.0604	13.5
	3	762	53.0	0.0610	12.6

	Average 803		50.5	0.0614	12.0

50.0	1	216	86.7	0.0427	38.9
	2	229	85.9	0.0399	42.9
	3	216	86.7	0.0384	45.0

	Average 220		86.4	0.0403	42.3

Source : MOE Japan
Test substance : 3,5,5-trimethyl-1-hexanol
 TOKYO KASEI KOGYO CO., LTD., Purity:93.8%
Reliability : (1) valid without restriction
 Well conducted study, carried out by Chemicals Inspection &
 Testing Institute, Japan
Flag : Critical study for SIDS endpoint
 05.01.2002

(6)

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 : m = 1.46
LOEC : m = 3.87
EC50 : m = 2.09
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : -Test Organisms:
a)Age at Study Initiation:<24 hours after hatching
b)Supplier/Source: Supplied from U.S. EPA Environmental Research Laboratory
-Test Condition:
a)Dilution Water Source: dechlorinated tap water
b)Dilution Water Chemistry: hardness = 55.6mg/L as CaCO₃, pH = 7.7, chlorine concentration <0.02 mg/L
c)Exposure Vessel Type: 1.8 L test solution in 3.0L glass vessel (diameter = 16 cm, depth = 17 cm)
d)Nominal Concentration(as mg/L): 0.128-5.00 (Nominal concentration << water solubility(450 mg/L))
e)Vehicle/Solvent and Concentrations: Vehicle;hydrogenated castor oil(HCO-40) 25.0mg/L, Solvent;Not used
f) Stock Solutions Preparations and Stability: A proportional diluter system was used for intermittent introduction of test material solution (0.1 wt% of test chemical with solubilizer hydrogenated castor oil HCO-40 5000mg/L) and dilution and water into the test chambers.
g)Number of Replicates: 4
h)Individuals per Replicates: 10
i)Flow-through Rate : 50mL/min
j)Water temperature: 19-21 degree C
k)Intensity of Irradiation: room light
l)Photoperiod: 16h:8h light-dark cycle
m)Feeding: Daphids were fed green algae(*Chlorella vulgaris*);2-4x10E8 cells/L
-Duration of the Test: 21days
-Test Parameter: Not described
-Analytical Method: gas chromatography
-Statistical Method:
a)Data Analysis: Not described
b)Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean,geometric mean, etc): arithmetic mean described
Result : -Nominal/measured Concentration:

Nominal concentration (mg/L)	Measured concentration(mg/L) (percentage of nominal)				
	0-day	7-day	14-day	21-day	Mean*
Control	n.d.	n.d.	n.d.	n.d.	-
Solvent control	n.d.	n.d.	n.d.	n.d.	-
0.128	0.103 (80.1)	0.0854 (66.7)	0.0878 (68.6)	0.0860 (67.2)	0.0904 (70.7)
0.320	0.273 (85.4)	0.230 (71.9)	0.231 (66.5)	0.200 (62.5)	0.229 (71.5)
0.800	0.703 (87.9)	0.622 (77.7)	0.785 (98.1)	0.454 (56.8)	0.641 (80.1)
2.00	1.62 (80.8)	1.54 (76.8)	1.51 (75.3)	1.19 (59.3)	1.46 (73.0)

5.00 4.08 4.06 3.67 3.67 3.87
(81.6) (81.2) (73.5) (73.5) (77.4)

n.d. : <0.100 mg

*The values are express as arithmetic means calculated

-Effect Data (reproduction)

21 day LC50 > 3.87 mg/L

21 day ErC50 = 2.09 mg/L (95% c.i.: 1.94- 2.25 mg/L)

NOECr = 1.46 mg/L

LOECr = 3.87 mg/L

-Water Temperature: 19.9-20.3 degree C

-Water Chemistry in test: PH 7.3-7.6; DO = 8.3-8.9
mg/L(Oxygen saturation level>=60%)

-Cumulative number of dead parental Daphnia:

Measure Cumulative number of dead parental Daphnia
concentration Exposure time (day)

(mg/L) 1 2 3 4 5 6 7 8 9 10 11 12

Control 0 0 0 0 0 0 0 0 0 0 0 0
(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

Solvent control

0 0 0 0 0 0 0 0 0 0 0 0
(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

0.0904 0 0 0 0 0 0 0 0 0 0 0 0

(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

0.229 0 0 0 0 0 0 0 0 0 0 0 0

(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

0.641 0 0 0 0 0 0 0 0 0 0 0 0

(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

1.46 0 0 0 0 0 0 0 0 0 0 0 0

(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

3.87 0 0 0 0 0 0 0 0 0 0 0 0

(0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)

(mg/L) 13 14 15 16 17 18 19 20 21

Control 0 0 0 0 1 2 4 5 6
(0) (0) (0) (0) (2.5) (5.0) (10.0) (12.5) (15.0)

Solvent control

0 0 0 0 1 2 5 7 7
(0) (0) (0) (0) (2.5) (5.0) (12.5) (17.5) (17.5)

0.0904 0 0 0 1 1 1 2 2 4

(0) (0) (0) (2.5) (2.5) (2.5) (5.0) (5.0) (10.0)

0.229 0 0 0 1 3 3 8 12 13

(0) (0) (0) (2.5) (7.5) (7.5) (20.0) (30.0) (32.5)

0.641 0 0 0 0 0 1 1 2 5

(0) (0) (0) (0) (0) (2.5) (2.5) (5.0) (12.5)

1.46 0 1 1 1 1 2 3 4 5

(0) (2.5) (2.5) (2.5) (2.5) (5.0) (7.5) (10.0) (12.5)

3.87 3 3 3 3 3 3 3 4 5

(7.5) (7.5) (7.5) (7.5) (7.5) (7.5) (7.5) (10.0) (12.5)

The value in parentheses express mortality(%) of Daphnia

-Time (days) required to first blood production during

exposure

Measure concentration (mg/L)	Vessel No.				Mean
	1	2	3	4	
Control	7	7	7	7	7.0
0.0904	7	7	7	7	7.0
0.229	7	7	7	7	7.0
0.641	7	7	7	7	7.0
1.46	7	7	7	7	7.0
3.87	10	10	10	10	10.0

-Mean cumulative number of Juvenile produced per adult during exposure:

Measure concentration (mg/L)	Exposure time (day)												
	1	2	3	4	5	6	7	8	9	10	11	12	
Control	0	0	0	0	0	0	0	4.4	4.4	4.4	38.0	38.0	42.6
Solvent control	0	0	0	0	0	0	0	5.3	5.3	5.3	38.0	38.0	41.0
0.0904	0	0	0	0	0	0	0	9.4	9.4	9.4	45.7	45.7	52.0
0.229	0	0	0	0	0	0	0	7.4	7.4	7.4	40.7	40.7	47.7
0.641	0	0	0	0	0	0	0	7.6	7.6	7.6	46.9	46.9	53.3
1.46	0	0	0	0	0	0	0	5.8	5.8	5.8	34.3	34.3	40.1
3.87	0	0	0	0	0	0	0	0	0	0	3.0	3.0	6.0
(mg/L)	13	14	15	16	17	18	19	20	21				
Control	42.6	85.0	85.0	85.0	138	138	188	188	197				
Solvent control	41.0	76.4	76.4	76.4	129	129	171	171	185				
0.0904	52.0	90.4	90.4	90.4	143	143	188	188	208				
0.229	47.7	89.8	89.8	89.8	133	133	176	176	206				
0.641	53.3	88.8	88.8	88.8	149	149	174	174	193				
1.46	40.1	60.0	60.0	60.0	108	108	128	128	135				
3.87	6.0	15.2	15.2	15.2	17.4	17.4	17.5	17.5	23.1				

Source : MOE Japan
Test substance : 3,5,5-Trimethyl-1-hexanol
 TOKYO KASEI KOGYO CO., LTD., Purity:93.8%
Reliability : (1) valid without restriction
 Well conducted study, carried out by Chemicals Inspection & Testing Institute, Japan
Flag : Critical study for SIDS endpoint
 05.01.2002

(8)

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

Species : other: *Xenopus laevis* (clawed toad)
Endpoint : mortality
Exposure period : 48 hour(s)
Unit : other: ug/l

LC50 : = 13500
Method : other: not specified
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : NOROXO Harnes
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
11.12.2001 (14)

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 : Sprague-Dawley
Sex : male/female
Number of animals : 5
Vehicle : other:Olive oil
Value : > 2000 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Result : No death occurred of either males or females and the LD50 was estimated to be more than 2000mg/kg. A decrease in spontaneous motor activity was observed on the day of administration, and body weight gains were suppressed or tended to be suppressed from days 1 to 14 of administration in males and females. No changes were detected on autopsy or histopathological examination.

LD50: Male,>2000mg/kg; female,>2000mg/kg

Source : MHW Japan
Test condition : -TEST ORGANISM
 a)Source :Japan Chales Liver Co.
 b)Number of animals/group: Males,5;females,5/group
 c)Weight at study initiation: 149-165 g for male
 126-144 g for female
 d)Age at study initiation: 5-6 weeks old for both sexes
 -ADMINISTRATION/EXPOSURE
 a)Vehicle: Olive oil
 b)Doses: 500,1000,2000 mg/kg
 c)Post dose observation period: 14 days
Test substance : SOURCE:KYOWA HAKKO KOGYO CO., LTD. Lot No.70713
 PURITY:92.7%

Reliability : (1) valid without restriction
 well conducted study, carried out by Safety Research
 Institute for Chemical Compounds Co., Ltd. (Japan)

Flag : Critical study for SIDS endpoint
 05.01.2002

(27)

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : ca. 2980 - 6400 mg/kg bw
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: various unspecified nonanols
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)

18.11.2001

(35)

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :

Vehicle :
Value : > 2979 mg/kg bw
Method : other: not specified
Year :
GLP : no data
Test substance : other TS
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
Test substance : Exxal 9 (isononyl alcohol, CAS# 68526-84-1). (19)
18.11.2001

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : = 3160 mg/kg bw
Method : other: not specified
Year :
GLP : no
Test substance : other TS: diisobutyl carbinol
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (24)

5.1.2 Acute inhalation toxicity

Type : LC50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 6 hour(s)
Value : > 730 ppm
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: various unspecified nonanols
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (34)

Type : LC50
Species : other: rat, mouse, guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 6 hour(s)
Value : > .065- .37 mg/L
Method : other: not specified
Year :
GLP : no data
Test substance : other TS
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
Test condition : Exxal 9 (isononyl alcohol, CAS# 68526-84-1) (21)
18.11.2001

5.1.3 Acute dermal toxicity

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : > 2960 mg/kg bw
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: various unspecified nonanols
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
 18.11.2001 (33)

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : > 3160 mg/kg bw
Method : other: not specified
Year :
GLP : no data
Test substance : other TS
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
Test substance : Exxal 9 (isononyl alcohol, CAS# 68526-84-1)
 18.11.2001 (20)

Type : LD50
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Value : > 10 mg/kg bw
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: unspecified nonanol
Source : NOROXO Harnes
 EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
 18.11.2001 (34)

5.1.4 Acute toxicity, other routes

5.2.1 Skin irritation

Species : rabbit
Concentration : undiluted
Exposure : Semiocclusive
Exposure time : 4 hour(s)

Number of animals : 6
PDII : 2.08
Result : moderately irritating
EC classification : irritating
Method : other: not reported
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : No animals died during the study. The test substance caused well-defined erythema in two of the six animals and mild erythema in the remaining animals at the 45 minute interval. At 24, 48, and 72 hours, 5 animals had well-defined erythema and 1 animal had mild erythema. By Day 7, only one animal had slight erythema. One animal at the 48 hour interval and 3 animals at the 72 hour interval had slight edema. By Day 7, desquamation was observed in all 6 animals.

Result : PII = 2.08
Mean erythema for 24, 48, and 72 hours: 1.83
Mean edema for 24, 48, and 72 hours: 0.22

Source : ExxonMobil Chemical
Test condition : Sex: Females
No. of animals: 6
route of administration: dermal
vehicle: NA
frequency of treatment: Single Dose
Dose/concentration levels: 0.5ml
Control group and Treatment: NA

The hair on the dorsal surface from the shoulder to the lumbar region of each rabbit was closely clipped with an electric clipper 24 hours prior to test substance administration. The skin was left intact. Each animal was fitted with an Elizabethan-type collar. During the study, animals were re-clipped as needed for dermal evaluations. Undiluted test material was applied as a single dose of 0.5ml. The application site was dressed with semi-occlusive dressing for the 4-hour exposure period. At the end of the exposure, the dressing was removed and residual test material was removed by reverse osmosis. The animals were examined for viability twice daily and dermal responses were evaluated approximately 45 minutes, 24, 48, and 72 hours following patch removal, and on Day 7. Scoring was according to the Draize method. GLP deviation: It is unknown whether the methods of synthesis, fabrication, and/or derivation of the test material were documented.

Conclusion : The test substance is considered a moderate irritant to rabbit skin.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.06.2002

(15)

5.2.2 Eye irritation

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure Time :
Comment :
Number of animals : 3
Result : moderately irritating
EC classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 2002

GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : All animals survived until study termination and were free of clinical signs during the study. Two distinct responses were observed in the animals. Two animals had no irritation or minimal conjunctival irritation that subsided by the 48-hour observation. No other responses were observed in these two animals. The remaining animal (1 out of 3) had moderate conjunctival and corneal irritation. Conjunctival irritation, consisting of redness and chemosis, was observed from the 1 through 72-hour observations. Discharge was observed at the 1, 48, and 72-hour observations. The corneal response, which consisted of opacity and ulceration, was observed from the 24 through 72-hour observations. Stippling was observed at the 72-hour observation. No signs of ocular irritation were observed in this animal at Days 7 and 10. The test substance is considered a moderate irritant to the rabbit eye.

Result : Maximum Draize: 18 out of 110; moderate irritant

Redness: 1hr (1.0), 24hr (1.0), 48hr (0.7), 72hr (0.7), Day 7(0), Day 10(0)
 Chemosis: 1hr (1.0), 24hr (0.3), 48hr (0.3), 72hr (0.3), Day 7(0), Day 10(0)
 Opacity: 1hr (0), 24hr (0), 48hr (0), 72hr (0.7), Day 7(0), Day 10(0)

Source : ExxonMobil Chemical
Test condition : One rabbit was initially treated with a volume of 0.1 ml of the test material. The right eye was treated and the left eye was used as an untreated control. The eyes were not irrigated. After consideration of the ocular response produced in the first animal, 2 additional animals were treated. Ocular irritation was assessed according to the Draize method approximately 1 hour and 24, 48, and 72 hours and on Days 7 and 10 following treatment.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
 24.06.2002

(22)

Species : rabbit
Concentration :
Dose :
Exposure Time :
Comment :
Number of animals :
Result : moderately irritating
EC classification : not irritating
Method : Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year : 1987
GLP : yes
Test substance : other TS: Isononyl Alcohol (Exxal 9)
Source : NOROXO Harnes

EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)

24.06.2002

(18)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure Time : 72 hour(s)
Comment :
Number of animals : 6
Result : moderately irritating
EC classification : not irritating
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1993
GLP : yes
Test substance : other TS:Isononyl Alcohol

Method	:	This study was performed to assess the irritation potential of Isononyl Alcohol in the eyes of New Zealand White Rabbits. The method used followed that described in the OECD Guidelines for Testing of Chemicals (1087) No. 405 "Acute Eye Irritation/Corrosion" referenced as Method B5 in Commission Directive 84/449/EEC
Result	:	A dulling of the normal luster of the corneal surface was noted in two treated eyes one hour after treatment. Diffuse corneal opacity was noted in five treated eyes at the 24, 48 and 72-hour observations. No other corneal effects were noted. Iridial inflammation was noted in two treated eyes one hour after treatment and in five treated eyes at the 24-hour observation. The effect persisted in four treated eyes at the 48-hour observation and in two treated eyes at the 72-hour observation. No other iridial effects were noted. Minimal to moderate conjunctival irritation was noted in all treated eyes one and 24 hours after treatment and in five treated eyes at the 48 and 72 hour observations. Petechial haemorrhage of the nictitating membrane was noted in one treated eye one hour after treatment. Treated eyes appeared normal 48 hours or seven days after treatment.
Source	:	ExxonMobil Chemical
Test condition	:	Immediately before the start of the test, both eyes of the six provisionally selected test rabbits were examined for evidence of ocular irritation or defect with the aid of a light source from a standard ophthalmoscope. Animals showing evidence of ocular lesions were rejected and replaced.
Test substance	:	Isononyl Alcohol CAS# 68526-84-1
Conclusion	:	The test material, Isononyl, produced a maximum group mean score of 23.2 and was classified as a moderate irritant (class 5 on a 1 to 8 scale) to the rabbit eye according to a modified Kay and Calandra classification system.
Reliability	:	(1) valid without restriction
Flag	:	confidential
24.06.2002		
Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	
Comment	:	
Number of animals	:	6
Result	:	moderately irritating
EC classification	:	not irritating
Method	:	other
Year	:	1968
GLP	:	no
Test substance	:	other TS:Isononyl Alcohol
Method	:	A single application of 0.1 ml of undiluted Isononyl Alcohol was instilled into the conjunctival sac of the left eye of 6 rabbits. Prior to application, the eyes were judged free of irritation and corneal damage (confirmed by sodium fluorescein examination). Treated eyes were held closed for one second following application. Untreated eyes served as controls. Observations for gross signs of eye irritation were made at 1, 4, 24, 48, and 72 hours, and at 4 and 7 days following application and at 10 days for animals whose eyes were not clear by 7 days. Eye irritation was scored according to the Draize method.
Result	:	Maximum group mean score: 23.2; 24h: 23.2; 48h: 17.7; 72h: 12.3. A single application of Isononyl Alcohol produced marked conjunctival irritation and slight iritis in all eyes. Corneal dullness followed after 4 or 24 hours postop with slight to marked corneal opacity in 5 of the 6 eyes. A rough-appearing cornea opacity was noted in 1 eye from day 2 through day 4 and in a second eye at day 7 only. The conjunctival irritation gradually diminished in intensity and completely subsided by day 7 in two eyes and by day 10 in the remaining eyes, and the iritis cleared by day 2 or day 4. In one eye, corneal opacity (slight) was present at 24 hours only, while the

(36)

remaining four eyes showed opacity until day 7 or day 10. Terminal Fluorescein Examination - On Day 7 or Day 10, negative for all treated eyes.

Source : ExxonMobil Chemical
Test substance : Isononyl Alcohol CAS# 68526-84-1
Reliability : (1) valid without restriction
Flag : confidential
24.06.2002 (23)

5.3 Sensitization

5.4 Repeated dose toxicity

Species : rat
Sex : male/female
Strain : Crj: CD(SD)
Route of admin. : gavage
Exposure period : Males;46days, Females;from14days before mating to day 3 of lactation
Frequency of treatment : Once daily
Post obs. period : none
Doses : 0(vehicle), 12,60,300mg/kg/day
Control group : yes, concurrent vehicle
NOAEL : = 12 mg/kg bw
LOAEL : = 60 mg/kg bw
Method : OECD combined study TG422
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Therefore, biochemical and haematological analysis, and urinalysis for females were not performed.
Result : -NOAEL (NOEL)
Male: 12 mg/kg/day, Female: 12 mg/kg/day

-Death:
In the 300 mg/kg group one female died on day 21 of gestation, and three others had to be killed because of weakness from days 14 to 19 of gestation. In these animals, body weights and food consumption were decreased, and histopathological examination revealed periportal fatty change in the liver, renal epithelial fatty change and other lesions.
-Body Weights Change and Food Consumption:
Food consumption was increased and body weights tended to be increased in males of the 300 mg/kg group, but the opposite was the case for females receiving the highest dose.
-Hematology,biochemistry and Urinalysis:
Urinalysis, hematological and biochemical examinations revealed increases in urine volume and water consumption and slight decreases in red blood cell counts, hematocrit, hemoglobin concentrations, BUN and chloride in males of the 300 mg/kg group.
-Organ weights:
Absolute liver weights were increased in males and females of the 300 mg/kg group, relative liver weights were increased in males and females of the 60 and 300 mg/kg groups, absolute and relative weights of the right and left kidneys were increased in males of the 60 and 300 mg/kg groups, and relative weights of the right and left kidneys were increased in females of the 300 mg/kg group.

-Autopsy:

Autopsy revealed pale discoloration of the kidneys in males of the 60 and 300 mg/kg groups, swelling of the kidneys in males of the 300 mg/kg group, and yellowish white discoloration of the liver in females of the 300 mg/kg group.

-Histopathology:

Histopathological examination revealed in male of the more than 12 mg/kg group, a slight or moderate degree of hyaline droplet and eosinophilic body in proximal tubular epithelium in kidney, but these findings were not observed in female (alpha2u-Globulin Nephropathy). A slight or moderate degree of renal tubular epithelial regeneration and formation of granular casts in kidneys in males of the 60 and 300 mg/kg groups, a slight degree of irregularity in the shape of follicles, columnar change of follicular epithelium and decrease in colloid in the thyroid were observed in males of the 300 mg/kg group. In female rats, a slight degree of renal epithelial fatty change in females of the 60 and 300 mg/kg groups, and atrophy of the thymus in the 300 mg/kg group.

Alpha2u-Globulin Nephropathy appears to be sex- and species-specific. That is, it occurs in male rats but not female rats and in mice, rabbit, guinea pigs or human. because they do not produce alpha2u-Globulin.

On the basis of these findings, the NOEL of 3,5,5-trimethylhexan-1-ol for repeat dose toxicity was considered to be 12 mg/kg/day for males and for females.

(Haematology)

Dose level(mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
Hematocrit(%)	52.6	52.6	52.4	49.9*
	±1.89	±2.90	±2.59	±2.25
Hemoglobin(g/dl)	16.4	16.2	15.7	15.3**
	±0.63	±0.68	±0.68	±0.68

(Blood chemical)

Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
BUN(mg/dl)	15.67	15.63	16.22	13.87*
	±1.87	±1.45	±1.66	±1.89
Cl(mEq/l)	107.3	106.5	106.2	104.8**
	±1.3	±2.4	±1.6	±0.6

(Organ weights)

<Males>:

Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
Absolute organ weight				
Liver(g)	12.120	12.953	13.676	17.815**
	±1.468	±2.178	±1.136	±1.723
Kidney(right,g)	1.570	1.602	1.771*	1.918**
	±0.120	±0.166	±0.196	±0.205
Kidney(left,g)	1.540	1.58	1.744**	1.906**
	±0.092	±0.184	±0.186	±0.232
Relative organ weight				
Liver(g%)	2.431	2.559	2.780**	3.493**
	±0.162	±0.227	±0.126	±0.207
Kidney(right,g%)	0.316	0.318	0.362*	0.378**
	±0.018	±0.022	±0.043	±0.043
Kidney(left,g%)	0.310	0.317	0.357**	0.375**

±0.018 ±0.031 ±0.043 ±0.053

<Females>:

	0	12	60	300
Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
Absolute organ weigh				
Liver(g)	13.222	13.470	14.384	16.032**
	±1.105	±1.142	±1.673	±1.340
Relative organ weight				
Liver(g%)	4.011	4.056	4.408*	5.330**
	±0.191	±0.219	±0.425	±0.390
Kidney(right,g%)	0.299	0.299	0.295	0.330*
	±0.050	±0.016	±0.022	±0.030
Kidney(left,g%)	0.295	0.289	0.291	0.328*
	±0.052	±0.019	±0.025	±0.036

Values are expressed as Mean±S.D.
Significantly different from 0mg/kg group
*,p<0.05, **,p<0.01

(Histopathology)

<Males>:

	0	12	60	300
Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
Kidney				
Hyaline droplet, proximal tubular epithelium				
	1	9**	12**	12**
Eosinophilic body, proximal tubular epithelium				
	0	9**	11**	12**
Regeneration, tublar epithelium				
	0	1	6*	7*
Cast, granular	0	0	3	6*
Thyroid				
Decrease, colloid	0	0	0	4

<females>:

	0	12	60	300
Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
Kidney				
Hyaline droplet, proximal tubular epithelium				
	0	0	0	0
Eosinophilic body, proximal tubular epithelium				
	0	0	0	0
Degeneration,fatty,proximal tubular epithelium				
	-	-	-	3
Thyroid				
Decrease, colloid	0	0	0	0
Thymus				
Atrophy	-	-	-	3

Values are no. of animals with findings.
Significantly different from 0mg/kg group
*,p<0.05, **,p<0.01

Source
Test condition

: MHW Japan
: -TEST ORGANISMS
a)Age:10week old
b)Weight at study initiation:335-399g for males,204-260g for females
c)Number of animals: 12 per sex per dose group
-ADMINISTRATION/EXPOSURE
a)Vehicle: Olive oil

		<p>b)type of exposure: oral feed by tube to stomach -SATELLITE GROUPS AND REASON THEY WERE ADDED: none -CLINICAL OBSERVATION AND FREQUENCY a)General condition was observed once a day. b)Body weight and food/water consumption were determined once a week. c)Hematology,biochemistry and urinalysis for males only at time of necropsy after 46 days of chemical exposure.</p> <p>-ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC) a)Macroscopic: organ weight: liver, kidney, adrenal, thymus, testes,(epidymis) b)Microscopic,Fall animals.</p>	
Test substance	:	SOURCE:KYOWA HAKKO KOGYO CO., LTD. Lot No.70713 PURITY:92.7%	
Reliability	:	(1) valid without restriction well conducted study, carried out by Safety Research Institute for Chemical Compounds Co., Ltd.(Japan)	
Flag 05.01.2002	:	Critical study for SIDS endpoint	(28)
Species	:	rat	
Sex	:	male	
Strain	:	Wistar	
Route of admin.	:	gavage	
Exposure period	:	14 days	
Frequency of treatment	:	daily	
Post obs. period	:		
Doses	:	144 mg/kg	
Control group	:	yes	
NOAEL	:	> 144 mg/kg bw	
Method	:	other: not specified	
Year	:		
GLP	:	no data	
Test substance	:	as prescribed by 1.1 - 1.4	
Result	:	In this study, trimethylhexanol did not induce testicular atrophy, hepatomegaly, peroxisome proliferation, or hypolipidemia in male rats.	
Source	:	NOROXO Harnes EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)	
Reliability 11.12.2001	:	(4) not assignable	(32)
Species	:	rabbit	
Sex	:	no data	
Strain	:	no data	
Route of admin.	:	dermal	
Exposure period	:	50 of 75 total days	
Frequency of treatment	:	daily for 1 hour exposure	
Post obs. period	:		
Doses	:	5 ml/day	
Control group	:	no data specified	
NOAEL	:	< 5	
Method	:	other: not specified	
Year	:		
GLP	:	no data	
Test substance	:	other TS: nonanol rich in trimethylhexanol	
Result	:	Contact on 5 ml on nonyl alcohol for 1 hour/day with skin of rabbits for each of 50 days over a period of 75 days resulted in RETARDED GROWTH AND ERYTHEMA, but no mortality.	
Source	:	NOROXO Harnes	

	EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)	
Reliability 11.12.2001	: (4) not assignable	(34)
Species	: rabbit	
Sex	: no data	
Strain	: no data	
Route of admin.	: oral unspecified	
Exposure period	: 67 of 83 days	
Frequency of treatment	: daily	
Post obs. period	:	
Doses	: 148 mg/kg/day	
Control group	: no data specified	
NOAEL	: > 148 mg/kg	
Method	: other: not specified	
Year	:	
GLP	: no data	
Test substance	: other TS: nonanol rich in trimethylhexanol	
Source	: EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)	
Reliability 11.12.2001	: (4) not assignable	(34)

5.5 Genetic toxicity 'in vitro'

Type	: Bacterial reverse mutation assay
System of testing	: <i>Salmonella typhimurium</i> , TA100, TA1535, TA98, TA1537, <i>Escherichia coli</i> Wp2 uvrA
Concentration	: TA1535, WP2uvrA, TA98: 15.6-500 ug/plate TA100, TA1537: 6.25-200 ug/plate
Cycotoxic conc.	:
Metabolic activation	: with and without
Result	: negative
Method	: other: Guidelines for screening Mutagenicity testing of Chemicals (Japan) and OECD Rest Guideline 471 and 472
Year	: 1997
GLP	: yes
Test substance	: as prescribed by 1.1 - 1.4
Result	: This chemical did not induce mutations in the <i>S. typhimurium</i> and <i>E. coli</i> strains. Toxicity was observed at 150 u/plate (TA100, TA1537), 250 ug/plate (TA1535, TA98, WP2) without an S9 mix, and at 150 ug/plate (TA100, TA1537), 250 ug/plate (TA1535, TA98), 500 ug/plate (WP2) with an S9 mix.
	Genetic effects: <i>Salmonella typhimurium</i> TA100, TA1535, TA98, TA1537 Without metabolic activation: negative With metabolic activation: negative <i>Escherichia coli</i> WP2 uvrA Without metabolic activation: negative With metabolic activation: negative
Source	: MHW Japan
Test condition	: Procedures : Pre-incubation method Solvent : DMSO Positive controls : -S9 mix, 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (TA100, TA98, WP2), Sodium azide (TA1535) and 9-Aminoacridine (TA1537)

		+S9 mix, 2-Aminoanthracene (five strains)	
	Doses	: -S9 mix; 0, 6.25, 12.5, 25.0, 50.0, 100, 200 ug/plate (TA100, TA1537)	
		0, 15.6 - 500 ug/plate (TA1535, TA98, WP2)	
		+S9 mix;	
		0, 6.25- 200 ug/plate (TA100, TA1537)	
		0, 15.6- 500 ug/plate (TA1535, TA98, WP2)	
	S9	: Rat liver, induced with phenobarbital and 5,6-benzoflavone	
		Plates/test : 3	
		Number of replicates : 2	
Test substance	:	SOURCE:KYOWA HAKKO KOGYO CO., LTD. Lot No.70713	
		PURITY:92.7%	
Reliability	:	(1) valid without restriction	
		well conducted study, carried out by Hatano Research Institute, Food and Drug safety center(Japan)	
Flag	:	Critical study for SIDS endpoint	
	05.01.2002		(29)
Type	:	Chromosomal aberration test	
System of testing	:	CHL/IU cell	
Concentration	:	0.013, 0.025, 0.050, 0.10, 0.20 mg/ml	
Cycotoxic conc.	:	Toxicity was not observed up to 0.1mg/ml in continuous and short-term treatment with or without S9 mix.	
Metabolic activation	:	with and without	
Result	:	negative	
Method	:	OECD Guideline 473 "Genetic Toxicology: <i>In vitro</i> Mammalian Cytogenetic Test"	
Year	:	1997	
GLP	:	yes	
Test substance	:	as prescribed by 1.1 - 1.4	
Result	:	Structural chromosomal aberrations and polyploidy were not induced up to a maximum concentration of 0.10mg/ml on continuous treatment, and with short-term treatment, with and without an exogenous metabolic activation system.	
		Cytogenetic effects were not observed under the conditions of this experiment.	
		Genotoxic effects:	
		clastogenicity	
		Without metabolic activation: negative	
		With metabolic activation: negative	
		polyploidy	
		Without metabolic activation: negative	
		With metabolic activation: negative	
Source	:	MHW Japan	
Test condition	:	For continuous treatment, cells were treated for 24 or 48 hrs without S- 9mix. For short-term treatment, cells were treated for 6 hrs with and without S9mix. and cultivated with fresh media for 18 hrs.	
		Solvent :Dmethylsulfoxide	
		Positive Controls:Mitomycin C for continuous treatment Cyclophosphamide for short-term treatment	
	Doses	:0, 0.025, 0.050, 0.10, 0.20 mg/ml	
	S-9	:Rat liver,induced with phenobarbital and 5,6-benzoflavone	
	Plates/test	:2	

Test substance : * At dose 0.2mg/ml,Chlomosome analysis was not performed because of sever cytotoxicity.
SOURCE:KYOWA HAKKO KOGYO CO., LTD. Lot No.70713
PURITY:92.7%

Reliability : (1) valid without restriction
well conducted study, carried out by Hatano Research Institute, Food and Drug safety center(Japan)

Flag : Critical study for SIDS endpoint
05.01.2002 (30)

5.6 Genetic toxicity 'in vivo'

5.7 Carcinogenity

5.8 Toxicity to reproduction

Type : other:OECD TG 422- Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test

Species : rat

Sex : male/female

Strain : Crj: CD(SD)

Route of admin. : gavage

Exposure period : Male; 46days, Female; from 14days before mating to day 3 of lactation

Frequency of treatment : once daily

Premating exposure period

Male : 14 days

Female : 14 days

Duration of test : male:46 days ; Female;from 14days before mating to day 3 of lactation

Doses : 0 (vehicle),12,60,300 mg/kg/day

Control group : yes, concurrent vehicle

NOAEL Parental : = 12 mg/kg bw

NOAEL F1 Offspr. : = 12 mg/kg bw

Method : OECD combined repeated dose and reproductive/developmental toxicity screening test

Year : 1997

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Remark : Deviations from Guideline: This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Estrous cycle length and pattern, and anogenital distances were not performed because the test was conducted by the TG adopted in 1990.

Result : NOAEL(NOEL): Male:300mg/kg/day; Female:60mg/kg/day
F1 gen.:12mg/kg/day
LOAEL(LOEL): Female:300mg/kg(estrous cycle examination)
F1 gen.:60mg/kg

<Reproductive and developmental toxicity>
As for the reproductive ability of parental animals, no effects were detected in any dose group in males. In females Prolongation of diestrous phase and decrease in implantation rate were observed in the 300 mg/kg group. Total litter loss in two dams of the 300 mg/kg group was observed. The number of pups born alive were decreased in the 60 and 300 mg/kg groups. With regard to the effects on neonates, viability on day 4 of lactation was decreased in the 300 mg/kg group, and male and female pups of the 300

mg/kg group showed lower body weights on day 0 of lactation.

(Reproduction Toxicity)				
Dose level (mg/kg/day)	0	12	60	300
No. of animals	12	12	12	12
No. of pregnant	11	11	12	11
No. of dead, sacrificed	0	0	0	4
No. of examined	11	11	12	7
Duration of mating (days, Mean±S.D.)				
	3.4	3.3	2.6	4.2
	±1.6	±0.9	±0.9	±3.4
Copulation index(%) (a)				
No. of implantation sites				
	15.8	15.0	14.3	13.4*
	±1.7	±1.5	±1.8	±2.1
Implantation index (%) (b)				
	97.4	91.5	88.2*	85.0*
	±3.8	±9.8	±12.0	±14.5
No. of pups born(%)				
	14.9	14.3	12.6	11.7*
	±1.8	±2.1	±2.3	±3.3
Live pups born				
No.				
	14.8	14.2	12.5*	10.1**
	±1.7	±2.0	±2.4	±2.7
Live birth index(%) (c)				
	99.4	99.5	99.2	88.9
	±1.9	±1.7	±2.6	±18.4
Sex ratio (M/F)				
	1.29	1.12	0.81**	1.53
	±0.48	±0.69	±0.37	±0.93
Live pups on day 4				
No.				
	14.5	14.0	12.0*	6.6**
	±1.9	±1.9	±2.4	±5.1
Viability index(%) (d)				
	98.0	98.8	96.3	64.9**
	±3.4	±2.6	±8.4	±64.9

Values are expressed as Mean±S.D.

Significantly different from 0mg/kg group

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

(a): (No. of pairs with successful copulation/no. of pairs mated)x100

(b): (No. of implantation sites/no. of corpora lutea)x100

(c): (No. of live pups born/no. of pups born)x100

(d): (No. of live pups on day 4/no. of live pups born)x100

On the basis of these findings, NOELs of 3,5,5-trimethylhexan-1-ol for reproductive/developmental toxicity were considered to be 300 mg/kg/day for males, 60 mg/kg/day for females, and 12 mg/kg/day for the F1 generation, respectively.

Source
Test condition

: MHW Japan
: TEST ORGANISMS
-Ages: 10 week old for both sexes
-Weight at study initiation: 335-399g for male, 204-260g for females
-Number of animals: 12 per sex per dose group
ADMINISTRATION/EXPOSURE
-Vehicle: Olive oil
-Satellite Groups and reasons they were added: none
-Mating Procedures: Male/female per cage; 1/1
PARAMETERS ASSESSED DURING STUDY:
-Clinical observation performed and frequency;

Parent:General appearance once a day.
Foetus:General appearance once a day after birth.
Hematology and biochemistry for males conducted only at time of necropsy after 46 days of chemical exposure.
Urinalysis was done on day 43 or 44 of the administration for male.
-Organs examined at necropsy
Parent:organ weight:liver, kidney, adrenal, thymus, testes, epididymis.
Microscopic: all animals: liver ,kidney, spleen, heart, lung, brain, pituitary gland, thymus, adrenal, tyroid, stomach, small intestine, appendix, large intestine, prostate gland and ovary. testes and.
Foetal:all macroscopic examination of all pups.
-Parameters assessed during study:
Body wt.(once a week), food/water consumption(once a week),
No. of pairs with successful copulation,copulation index (No. of pairs with successful copulation/No. of pairs mated x100)

Test substance : SOURCE:KYOWA HAKKO KOGYO CO., LTD. Lot No.70713
PURITY:92.7%

Reliability : (1) valid without restriction
well conducted study, carried out by Safety Research
Institute for Chemical Compounds Co., Ltd.(Japan)

Flag : Critical study for SIDS endpoint
05.01.2002 (28)

5.9 Developmental toxicity/teratogenicity

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : gestation days 1 -19
Frequency of treatment : 7 hours/day
Duration of test : 19 days
Doses : 25 ppm
Control group : yes
NOAEL Maternalt. : > 25 ppm
NOAEL Teratogen : > 25 ppm
Method : other: not specified
Year :
GLP : yes
Test substance : other TS: n-nonanol
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)

18.11.2001 (31)

Species : rat
Sex : female
Strain : no data
Route of admin. : gavage
Exposure period : Gestation days 6-15
Frequency of treatment : daily
Duration of test :
Doses : 144, 720, or 1440 mg/kg/day
Control group : yes
NOAEL Maternalt. : = 144 mg/kg bw
NOAEL Teratogen : = 144 mg/kg bw
Method : other: not specified
Year :
GLP : no data

Id 3452-97-9
Date 24.06.2002

Test substance : other TS: isononyl alcohol
Remark : Clear signs of maternal toxicity were seen at 720 and 1440 mg/kg/day.
Source : NOROXO Harnes
EUROPEAN COMMISSION- European Chemicals Bureau Ispra (VA)
18.11.2001 (37)

5.10 Other relevant information

5.11 Experience with human exposure

- (1) Bridie A.L., *Water Res.*(1979) 13,No 7. pp.327-30
- (2) Bridie et. al. (1979). The acute toxicity of some petrochemicals to goldfish. *Water Res.* 13(7), 623-626.
- (3) Chemical Inspection and Testing Institute, Japan, Report No. 81258K
- (4) Chemicals Evaluation and Research Institute(CERI), Japan (2001),unpublished data.
- (5) Chemicals Inspection & Testing Institute, Japan (1996) Report No. 21258
- (6) Chemicals Inspection & Testing Institute, Japan (1997) Test No. 91736
Ministry of Environment, Japan
- (7) Chemicals Inspection & Testing Institute, Japan (1997) Test No. 91737
Ministry of Environment, Japan
- (8) Chemicals Inspection & Testing Institute, Japan (1997) Test No. 91738
Ministry of Environment, Japan
- (9) Chemicals Inspection & Testing Institute, Japan (1997) Test No. 91739
Ministry of Environment, Japan
- (10) Chemicals Inspection & Testing Institute, Japan (1997) Test No. 91740
Ministry of Environment, Japan
- (11) Chemicals Inspection & Testing Institute, Japan (1998) Report No. 51258
- (12) Chemicals Inspection & Testing Institute, Japan.(2001) Report No. 81258 III K
- (13) Chemicals Inspection & Testing Institute, Japan.(1997) Report No. 81258K
- (14) DeZwart, D. and Slooff, W. (1987). Toxicity of mixtures of heavy metals and petrochemicals to *Xenopus laevis*. *Bull. Environ. Contam. Toxicol.* 38(2), 345-351.
- (15) EBSI, 1992. Primary Dermal Irritation Study in the Rabbit
- (16) Exxon Chemical Safety Data Sheet, Jan. 23, 1994.
- (17) Exxon Chemical Safety Data Sheet, January 23, 1994.
- (18) Exxon unpublished report number 93MRL 169. Exxal 9 (C9 Alcohol): Acute Eye Irritation Test in the Rabbit. Project Number 616/1. Conducted by SafePharm Laboratories, UK.
- (19) Exxon unpublished reports on Exxal 9: 68MRL 20, 78MR R600, 80MRL 135.
- (20) Exxon unpublished studies on Exxal 9: 68MRL 20, 78MRR 625
- (21) Exxon unpublished studies on Exxal 9: 80MRR 2320, 80MRL 37, 78MRL 51).
- (22) ExxonMobil Biomedical Sciences, 2002. Acute Eye Irritation Test
- (23) Hazleton Laboratories, Inc (1968) Acute Oral Administration - Rats, Acute Dermal Application - Rabbits, Acute Eye Application - Rabbits. Submitted report date May 20, 1968. Project No. 145-340.
- (24) *J. Ind. Hyg. Toxicol.* 31, p. 60 (1949).

6. REFERENCES

Id 3452-97-9
Date 24.06.2002

- (25) Kaczmarek, S. A. and Palis, J. C. BOD5/COD Determinations of Hazardous Chemicals, July 1981. Exxon reference 81ECD 1010.
- (26) Material Safety Data Sheet, KYOWA HAKKO KOGYO CO., LTD. 2001
- (27) Ministry of Health and Welfare: Japan (1997), Toxicity Testing Reports of Environmental Chemicals 5, 641-642
- (28) Ministry of Health and Welfare: Japan (1997), Toxicity Testing Reports of Environmental Chemicals 5, 643-659
- (29) Ministry of Health and Welfare: Japan (1997), Toxicity Testing Reports of Environmental Chemicals 5, 661-667
- (30) Ministry of Health and Welfare: Japan (1997), Toxicity Testing Reports of Environmental Chemicals 5, 669-672
- (31) Nelson et. al. (1990). *Tox. Ind. Health* 6(3-4), 373-387.
- (32) Rhodes et. al. (1984). The absence of testicular atrophy and *in vivo* and *in vitro* effects on hepatocyte morphology and peroxisomal enzyme activities in male rats following the administration of several alkanols. *Toxicol. Letts.* 21, 103-109.
- (33) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol. IIC, 3rd Revised Edition. Clayton and Clayton, eds. p.4626-4629.
- (34) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol. IIC, 3rd Revised Edition. Clayton and Clayton, eds. p. 4626-4629.
- (35) Rowe, V. K. and McCollister, S. B. (1982). Alcohols, in Patty's Industrial Hygiene and Toxicology, Vol. IIC, 3rd Revised Edition. Clayton and Clayton, eds. p. 4626-4629.
- (36) Safepharm Laboratories, LTD (1993) C9 Alcohol: Acute Eye Irritation Test in the Rabbit.. For Exxon Chemical International, Inc. Project No 616/1.
- (37) U.S. EPA/OTS: Document #89-910000247. TSCA Section 8(e) submission.
- (38) Veith et. al (1983). Structure-toxicity relationships for the fathead minnow, *Pimephales promelas*: Narcotic industrial chemicals. *Can. J. Fish Aquatic Sci.* 40, 743-748.
- (39) Yaw.C.L., Waste Management, Vol17 pp. 541-7, 1997

Appendix : Parameters used in calculation of distribution by Mackay Level III fugacity model.
(3452979-Appendix.doc)

Theoretical distribution of 3,5,5-Trimethyl-1-hexanol

Scenario 1

Compartment	Emission rate [kg/h]	Concentration [g/m ³]	Amount [kg]	Percent [%]	Transformation rate [kg/h]	
					Reaction [kg/h]	Advection [kg/h]
Air	1000	3.3.E-06	3.3.E+04	9.9	64.E+02	3.3.E+02
Water	0	1.0.E-03	2.1.E+04	6.2	6.0.E-02	2.1.E+01
Soil	0	1.7.E-01	2.8.E+05	83.1	8.1.E-01	
Sediment		2.7.E-02	2.7.E+03	0.8	2.6.E-03	5.3.E-02
Total amount			3.4.E+05			

Scenario 2

Compartment	Emission rate [kg/h]	Concentration [g/m ³]	Amount [kg]	Percent [%]	Transformation rate [kg/h]	
					Reaction [kg/h]	Advection [kg/h]
Air	0	1.1.E-06	1.1.E+04	1.3	2.2.E+02	1.1.E+02
Water	1000	3.3.E-02	6.6.E+05	77.6	1.9.E+00	6.6.E+02
Soil	0	6.0.E-02	9.5.E+04	11.1	2.7.E-01	
Sediment		8.5.E-01	8.5.E+04	9.9	8.1.E-02	1.7.E+00
Total amount			8.5.E+05			

Scenario 3

Compartment	Emission rate [kg/h]	Concentration [g/m ³]	Amount [kg]	Percent [%]	Transformation rate [kg/h]	
					Reaction [kg/h]	Advection [kg/h]
Air	0	1.5.E-06	1.5.E+04	0.0	2.8.E+02	1.5.E+02
Water	0	1.5.E-02	3.0.E+05	0.3	8.7.E-01	3.0.E+02
Soil	1000	5.7.E+01	9.1.E+07	99.6	2.6.E+02	
Sediment		3.9.E-02	3.9.E+04	0.0	3.7.E-02	7.7.E-01
Total amount			9.2.E+07			

Scenario 4

Compartment	Emission rate [kg/h]	Concentration [g/m ³]	Amount [kg]	Percent [%]	Transformation rate [kg/h]	
					Reaction [kg/h]	Advection [kg/h]
Air	600	2.5.E-06	2.5.E+04	0.3	4.8.E+02	2.5.E+02
Water	300	1.2.E-02	2.4.E+05	2.5	7.0.E-01	2.4.E+02
Soil	100	5.8.E+00	9.3.E+06	96.9	2.7.E+01	
Sediment		3.1.E-01	3.1.E+04	0.3	3.0.E-02	6.2.E-01
Total amount			9.6.E+06			

Compartment	Release 100% to air	Release 100% to water	Release 100% to soil
Air	9.9%	1.3%	0.0%
Water	6.2%	77.6%	0.3%
Soil	83.1%	11.1%	99.6%
Sediment	0.8%	9.9%	0.0%

(Continued)

Appendix : (Continued)

Physico-chemical parameter

Molecular weight	144.26	Measured
Melting point [°]	-70	Measured
Vapor pressure [Pa]	9.01E+00	Measured
Water solubility [g/m ³]	450	Measured
log Kow	3.42	Measured
Half lives [h] (Note 1)	In air	36
	In water	240000
	In soil	240000
	In sediment	720000

Temperature [°]	25
-------------------	----

Environmental parameter

		Volume [m ³]	Depth [m]	Area [m ²]	Organic carbon content [-]	Lipid content [-]	Density [kg/m ³]	Residence Time [h]
Bulk air	Air	1.0E+13					1.2	100
	Particles	2.0E+03						
	Total	1.0E+13	1000	1E+10				
Bulk water	Water	2.0E+10					1000	1000
	Particles	1.0E+06			0.04		1500	
	Fish	2.0E+05				0.05	1000	
	Total	2.0E+10	10	2E+09				
Bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1000	
	Solid	8.0E+08			0.04		2400	
	Total	1.6E+09	0.2	8E+09				
Bulk Sediment	Water	8.0E+07					1000	
	Solid	2.0E+07			0.06		2400	50000
	Total	1.0E+08	0.05	2E+09				

Intermedia transport parameter

[m/h]

Air side air-water MTC	5	Soil air boundary layer MTC	5
Water side air-water MTC	0.05	Sediment-water MTC	1E-04
Rain rate	1E-04	Sediment deposition	5E-07
Aerosol deposition	6E-10	Sediment resuspension	2E-07
Soil air phase diffusion MTC	0.02	Soil water runoff	5E-05
Soil water phase diffusion MTC	1E-05	Soil solid runoff	1E-08