FOREWORD INTRODUCTION

1,3,5-TRIAZINE-2,4,6(1H,3H,5H)-TRIONE,1,3,5-TRIS(2HYDROXYETHYL)

CAS N°: 839-90-7

SIDS Initial Assessment Report for 14th SIAM

(Paris, 26-28th March 2002)

Chemical Name: 1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-

CAS No: 839-90-7

Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:
Mr. Yasuhisa Kawamura,
Ministry of Foreign Affairs, Japan

History: The chemical is sponsored by Japan under ICCA initiative and is submitted for first discussion at SIAM.

Peer review Process:
Ministry of Health, Labour and Welfare, Ministry of Economy, Trade and Industry and Ministry of Environment peer-reviewed the documents, audited selected studies.

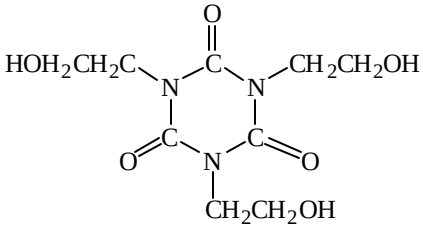
Testing: No testing (X) Testing ( )

Comments:
ICCA Initiative work lead by NISSAN CHEMICAL INDUSTRIES, LTD., Japan.
SIDS Initial Assessment Documents were prepared by Chemicals Evaluation and Research Institute (CERI), Japan.

Deadline for Circulation: 01/02/2002

Date of Circulation: 01/02/2002

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	839-90-7
Chemical Name	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)- (Synonym : Tris(2-hydroxyethyl) isocyanurate)
Structural Formula	

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Regarding acute toxicity, the oral LD_{50} of tris(2-hydroxyethyl) isocyanurate in rats is greater than 2,000 mg/kg bw [OECD TG 401]. The acute dust inhalation toxicity test for 8h in rat revealed no symptom and no mortality at 9.32 mg/L and 15 mg/L. Tris(2-hydroxyethyl)isocyanurate is not irritant to eye and skin. No data are available for sensitization.

In the combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] in rats, which was performed at oral doses of 0, 30, 100, 300 and 1,000 mg/kg bw/day for at least 42 days, no deaths or abnormalities in all toxicological parameters were observed in any male and female animals. The NOAEL for repeated dose toxicity in rats is considered to be 1,000 mg/kg bw/day for both sexes.

In the above combined repeated dose and reproductive/developmental toxicity test in rats, the chemical showed no adverse effects on any reproductive/developmental parameters. No morphological abnormalities in external and visceral observation in pups were observed in any of the treated groups. The NOAEL values in reproductive/developmental toxicity for both parents and F_1 offspring are considered to be 1,000 mg/kg bw/day.

Bacterial mutation test [OECD TG 471] and all mammalian *in vitro* tests such as chromosome aberration tests [OECD TG 473 & NTP] and sister chromatid exchange assay [NTP] showed negative results. There is no data available from *in vivo* test.

Environment

As for the distribution of the chemical in the environmental, Fugacity model (level III) calculation shows that the chemical is likely to be distributed into water and soil if released into water, air or soil. Also, based on its high water solubility (820 g/L at 20°C), low LogPow value (-1.63 at 23°C) and low vapor pressure (0.0015 Pa at 50°C), the chemical is most likely distributed into the water phase. The half-life for photo-degradation is estimated to be 13.0 h. The chemical is highly stable in water (OECD TG 111) and is not biodegradable according to OECD test guidelines 301C (0%(BOD)), 301E and 302B (0%(DOC)), respectively. However, bioaccumulation potential of this substance is low based on the results of the bioaccumulation test using carp (*Cyprinus carpio*). In the test, the resulting BCF values were below 0.16 at 2.5 mg/L or 1.6 at 0.25 mg/L of test concentration, respectively.

The acute toxicity values to aquatic organisms were more than 1,000 mg/L for *Selenastrum capricornutum* (72h-NOEC, biomass and growth rate), greater than 1,000 mg/L for *Daphnia magna* (48h-EC_{50}, immobilization) and greater than 100 mg/L for *Oryzias latipes* (96h-LC_{50}, mortality) according to OECD TG 201, 202 and 203, respectively. In the chronic toxicity test to *Daphnia magna*, the 21d-NOEC (reproduction) was more than 100 mg/L (OECD TG 211). As no adverse effects were observed in any tests conducted using three different trophic level species, the chemical is considered to be non-toxic to aquatic organisms.

Exposure

The production volume of tris(2-hydroxyethyl) isocyanurate in 2000 was 6,000 tonnes in Japan and 5,000 tonnes in Germany. The production and the cleaning process of the facility are conducted in a closed continuous line under remote control system.

Mainly, the chemical is used as a monomer for the synthesis of polyesters and thus obtained polyesters are industrially used in thermosetting varnishes and thermosetting paints for metal. It is also used in polymer industry as a stabilizer. The content in polymers is approximately 0.5% or less. One of the uses of such polymers is as exterior building material.

The chemical would not be released into environment via wastewater from production or use (such as varnishes or paints industry) sites because organic solvent is used instead of water for the reaction media or cleaning process. Moreover, the solvent used is concentrated and then the residues are incinerated in a well-equipped facility. Releases from final polyester products are not expected. The chemical might be released from polymers which contain the chemical as a stabilizer. Although no data are available on the amount of the chemical used as a stabiliser, significant exposure is not expected.

The occupational exposure of the chemical might occur via the inhalation of dust or via the dermal route during packing/unpacking processes. However, the intake via dermal route is not expected due to the low value of the LogPow. Practically, workers are obliged to use personal protection equipment (mask, glasses and gloves) during the packing/unpacking process. Thus, the exposure to the chemical via dust inhalation is considered to be negligible.

Polymers containing the chemical as a stabilizer are the only source of the chemical which might cause consumer exposure and indirect exposure in the general population.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.

The chemical is not a candidate for further work because all SIDS endpoints are adequately addressed and the substance has a low toxicity profile.

FULL SIDS SUMMARY

CAS NO: 839-90-7		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		DIN 53 181	133-135 °C
2.2	Boiling Point		Unknown	296 °C (decomposed)
2.3	Density		Unknown	1.46 g/cm ^{3} at 20 °C
2.4	Vapor Pressure		Unknown	0.001 Pa at 50 °C
			Calculated (MONO5)	6.1 x 10^{-5} Pa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	-1.63 at 23 °C
2.6.1 A.	Water Solubility		Unknown	820 g/L at 20 °C
B.	pH			No data available.
	pKa			No data available.
2.12	Oxidation: Reduction Potential			No data available.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Calculated (AOPWIN Ver.1.90)	$T_{1/2}$ = 13.0 h (sensitizer: OH radical)
3.1.2	Stability in Water		OECD TG 111	Stable (at pH 4.0, 7.0 and 9.0)
3.2	Monitoring Data			No data available.
3.3	Transport and Distribution		Calculated (Fugacity Model, Level III)	[Release: 100 % to air] Air 0.0% Water 50.3% Soil 49.5% Sediment 0.2% [Release: 100% to water] Air 0.0% Water 99.6% Soil 0.0% Sediment 0.4% [Release: 100% to soil] Air 0.0% Water 44.6% Soil 55.2% Sediment 0.2%
3.5	Biodegradation		OECD TG301C	Not readily biodegradable in 14 days BOD: 0%, TOC: 2.5%, LC: 7.2%
			OECD TG 301E	Not readily biodegradable: 0 % (DOC) after 28 days
			OECD TG 302B	Not inherently biodegradable: 0 % (DOC) after 28 days
3.6	Bioaccumulation	*Cyprinus carpio* (carp)	OECD TG 305C	BCF: =<0.16 (2.5 mg/L) BCF: =<1.6 (0.25 mg/L)
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (96h, Mor*[1]): > 100 mg/L LC_{10} (96h, Mor*[1]): = 100 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (48h, Imm*[2]): > 1,000 mg/L EC_0 (48h, Imm*[2]): >= 1,000 mg/L

CAS NO: 839-90-7		SPECIES	PROTOCOL	RESULTS
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72h, Biomass and Grt* [3]): > 1,000 mg/L NOEC (72h, Biomass): >= 1,000 mg/L
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 211	EC_{50} (21d, Rep* [4]): > 100 mg/L LOEC (21d,Rep* [4]): > 100 mg/L NOEC (21d, Rep* [4]): >= 100 mg/L
4.6.1	Toxicity to Soil Dwelling Organisms			No data available.
4.6.2	Toxicity to Terrestrial Plants			No data available.
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} > 2,000 mg/kg
5.1.2	Acute Inhalation Toxicity			No mortality, no symptom and no necropsy findings were observed by the exposure to dust at 9.32 or 15 mg/L as nominal concentration in air for 8 hours.
5.1.3	Acute Dermal Toxicity			No data available.
5.4	Repeated Dose Toxicity	Rat	OECD TG 422	NOAEL: 1,000 mg/kg bw/day
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test (Gene mutation)	*S.typhimurium* *E.coli*	OECD TG 471 and Guidelines for Screening Mutagenicity Testing of Chemicals (Japan)	Negative (With metabolic activation) Negative (Without metabolic activation)
		S.typhimurium	NTP's mutagenic testing program	Negative (With metabolic activation) Negative (Without metabolic activation)
B.	Non-Bacterial *In Vitro* Test (Chromosomal aberrations)	CHL cells	OECD TG 473 and Guidelines for Screening Mutagenicity Testing of Chemicals (Japan)	Negative (With metabolic activation) Negative (Without metabolic activation)
		CHO cells	NTP's mutagenic testing program	Negative (With metabolic activation) Negative (Without metabolic activation)
C.	Non-Bacterial *In Vitro* Test (Sister chromatid exchange assay)	CHO cells	NTP's mutagenic testing program	Negative (With metabolic activation) Negative (Without metabolic activation)
5.6	Genetic Toxicity *In Vivo*			No data available.
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOAEL Parental: 1,000 mg/kg bw/day NOAEL F1 offspring:

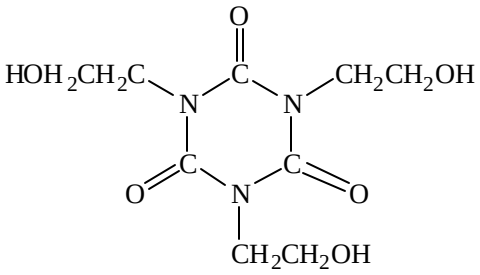
CAS NO: 839-90-7		SPECIES	PROTOCOL	RESULTS
				1,000 mg/kg bw/day
5.9	Developmental Toxicity/ Teratogenicity	Rat	OECD TG 422	NOAEL Maternal toxicity: 1,000 mg/kg bw/day NOAEL Teratogenicity: 1,000 mg/kg bw /day
5.11	Experience with Human Exposure			No data available.

*[1] Mor: Mortality, *[2] Imm: Immobility, *[3] Grt: Growth rate, *[4] Rep: Reproduction

SIDS INITIAL ASSESSMENT REPORT

1. IDENTITY

- Name (OECD): 1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-
- CAS number: 839-90-7
- Molecular formula: $C_9H_{15}N_3O_6$
- Structural formula:



- Molecular weight: 261.23
- Synonyms: Tris(2-hydroxyethyl) isocyanurate
  1,3,5-Tris(2-hydroxyethyl) isocyanurate
  1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-
  1,3,5-Tris(2-hydroxyethyl) isocyanuric acid
  Isocyanuric acid, tris(2-hydroxyethyl) ester
  N,N',N''-Tris(2-hydroxyethyl) isocyanurate
  s-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-
  s-Triazine-2,4,6(1H,3H,5H)-trione, tris(2-hydroxyethyl)-
  Tris(beta-hydroxyethyl) isocyanurate
  Tris(2-hydroxyethyl)-s-triazine-2,4,6-trione
  Tris(2-hydroxyethyl)isocyanurat
  Tris(hydroxyethyl) isocyanurate
  TANAC
  THEIC
  Theich
- Purity: 99 % (w/w)
- Major impurities: Bis(2-hydroxyethyl) isocyanurate (ca. 0.5 %)
  1,3-Bis(2-hydroxyethyl)-5-[[(2-hydroxyethyl)oxy]ethyl]-isocyanurate (ca. 0.5 %)
- Additives: None

- Physical-chemical properties:

	Protocol	Results
Melting point:	DIN 53 181	133 - 135 °C
Boiling point:	Unknown	296 °C (decomposed)
Density:	Unknown	1.46 g/cm^3 at 20 °C
Vapor pressure:	Unknown	0.001 Pa at 50 °C (measured)
	Calculated	6.1 x 10^{-5} Pa at 25 °C
Water solubility:	Unknown	820 g/L at 20 °C
Log Pow:	OECD TG 107	-1.63 at 23 °C
Koc:	Calculated	10

2. GENERAL INFORMATION ON EXPOSURE

The production volume of tris(2-hydroxyethyl) isocyanurate in 2000 was 6,000 tonnes in Japan and 5,000 tonnes in Germany (NISSAN CHEMICAL INDUSTRIES, LTD., 2001).
The production and the cleaning process of the facilities are conducted in a closed continuous line under remote control system (NISSAN CHEMICAL INDUSTRIES, LTD., 2001).
The chemical is mainly used as a monomer for the synthesis of polyesters and thus obtained polyesters are industrially used in thermosetting varnishes and thermosetting paints for metal. It is also used in polymer industry as a stabilizer. The content in polymers is approximately 0.5% or less. One of the uses of such polymers is as exterior building material. (NISSAN CHEMICAL INDUSTRIES, LTD., 2001).

Based on the high water solubility of the chemical, the chemical might be released into the environment from production or use sites (such as varnishes or paints industry) via wastewater. However, water is not used in the system because organic solvents are used instead of water as a reaction media or as a cleaning solvent for the system. Also, the solvent used is concentrated, and then the residue of the chemical is incinerated in a well-equipped facility. Thus, the release of the chemical into the environment from production or user sites is considered to be negligible.

The release of the chemical into the environment from thermosetting varnishes or thermosetting paints, which uses polyesters synthesized from the chemical, is considered to be negligible because most of the chemical is polymerized under controlled polymerization reaction and it is not expected that significant quantities of monomers remain in the final polyester products. The chemical might be released from polymers which contain the chemical as a stabilizer. However, no data are available on the amount of the chemical used as a stabilizer.

2.1 Environmental Fate

Tris(2-hydroxyethyl) isocyanurate has a low vapor pressure (0.001 Pa at 50 °C (measured), 6.1 x 10^{-5} Pa at 25°C (calculated)), a high water solubility (820 g/L at 20 °C) and is hydrophilic (Log Pow: -1.63 at 23 °C). Judging from its physico-chemical properties, the chemical released into the environment would be mainly distributed into the water compartment.
The chemical was stable in water at pH 4.0, 7.0 and 9.0 in a hydrolysis test according to OECD TG 111 (METI, Japan. Unpublished).
The half-life time of 13.0 h was calculated for the degradation of the chemical in air by the reaction with photochemically produced OH radical (CERI, 2001).
There were three reliable data on biodegradability. The chemical was not readily biodegradable according to OECD TG 301C [0 % (BOD), 2.5 % (TOC) and 7.2 % (LC) after 14 days] (METI, Japan. Unpublished) and OECD TG 301E [0 % (DOC, 28 days)] (BASF AG, 1990a). Also, according to OECD TG 302B, the test for inherent degradability resulted in 0 % (DOC) degradation after 28 days (BASF AG, 1990b), and suggested that the chemical was not inherently biodegradable.

The bioaccumulation test using carp (*Cyprinus carpio*) at the concentrations of 2.5 and 0.25 mg/L resulted in BCFs of below 0.16 and 1.6, respectively (METI, Japan. Unpublished).
The generic Fugacity model (level III) was employed to estimate the potential environmental distribution of tris(2-hydroxyethyl) isocyanurate in air, water, soil and sediment (CERI, 2001). The calculation results are shown in Table 1. The results show that when the chemical is released into water, the majority of the chemical likely remains in water, and that when released into air or soil, almost equal amount of the chemical is likely distributed into water and soil. However, the release into air is negligible due to its low vapor pressure. The chemical distributed into soil would not stay longer due to a low value of Koc (10 (calculated)).

Table 1. Environmental distribution of tris(2-hydroxyethyl) isocyanurate using a generic Fugacity model, Mackay level III.

Component	Release: 100 % to air	Release: 100 % to water	Release: 100 % to soil
Air	0.0 %	0.0 %	0.0 %
Water	50.3 %	99.6 %	44.6 %
Soil	49.5 %	0.0 %	55.2 %
Sediment	0.2 %	0.4 %	0.2 %

Thus, tris(2-hydroxyethyl) isocyanurate is mainly distributed into the water compartment based on its physical-chemical properties and the Fugacity model calculation. Although the substance is persistent in the environment, it has a low bioaccumulation potential.

2.2 Human Exposure

2.2.1 Occupational Exposure

While the chemical is produced in a closed system, occupational exposure to the chemical might occur via the dermal route or via the inhalation of dust during packing/unpacking processes. However, an intake via the dermal route is not expected because of the low value of the Log Pow (-1.63).
The chemical is produced as a non-fibrous powder and the atmospheric dust concentration is estimated to be 2-5 mg/m^3 by the EASE model assuming a dry method with local ventilation equipment during the packing/unpacking operation. The maximum EHE_{inh} of dust is expected to be 0.71 mg/kg bw/day for a 8-h work duration without personal respiratory protection (see appendix 1).
As for the exposure via vapor inhalation, it is considered to be negligible since the maximum vapor concentration in air of the chemical is calculated as 9.9×10^{-3} ppm from its vapor pressure (0.001 Pa at 50°C (measured)).
Practically, the chemical is operated in a closed system and workers are obliged to use personal protection equipments such as mask, safety glasses and gloves during the packing/unpacking processes. Thus, the exposure levels to the chemical via dermal or inhalation routes are considered to be negligible.

2.2.2 Consumer Exposure

The substance is mainly used for the synthesis of polyesters. Consumer exposure via final polyester products is negligible because most of the chemical is polymerized and residual contents of the chemical in products such as thermosetting varnishes or thermosetting paints for metal are not expected.
Consumer exposure is possible via the dermal route only by handling polymeric products containing the chemical as a stabilizer.

2.2.3 Indirect Exposure via the Environment

Indirect exposure of man via drinking water could occur since the chemical might be released into environment via products containing the chemical as a stabilizer. No data are available on the amount of the chemical used as a stabilizer.

3. EFFECTS ON THE ENVIRONMENT

3.1 Effects on Aquatic Organisms

Toxicity tests with tris(2-hydroxyethyl) isocyanurate were conducted to determine the acute toxicity to aquatic organisms (*Selenastrum capricornutum*, *Daphnia magna* and *Oryzias latipes*) according to OECD TG (201, 202 and 203, respectively) in compliance with GLP, and for the chronic toxicity to *Daphnia magna* according to OECD TG 211 in compliance with GLP (MOE, Japan, 2000). Acute and chronic toxicity data for the chemical are summarized in Table 2.
No significant effects were observed at the concentrations tested in any acute or chronic toxicity tests.

Table 2. Acute and chronic toxicity data of tris(2-hydroxyethyl) isocyanurate to aquatic organisms at different trophic levels.

Species	Endpoint[*1]	Method	Conc. (mg/L)	Reference
Selenastrum capricornutum (alga)	Biomass and Grt: EC_{50} (72h) Biomass and Grt: NOEC(72h)	OECD TG 201	>1,000 >=1,000	MOE, Japan (2000)
Daphnia magna (water flea)	Imm: EC_{50} (48h)	OECD TG 202	>1,000	
	Rep: EC_{50} (21d) Rep: NOEC (21d)	OECD TG 211	>100 >=100	
Oryzias latipes (fish, Medaka)	Mor: LC_{50} (96h) Mor: LC_{10} (96h)	OECD TG 203	>100 =100	

Notes: [*1] Grt; Growth rate, Imm; immobilisation, Rep; reproduction, Mor; mortality.

3.2 Terrestrial Effects

No data available.

3.3 Other Effects

No data available.

3.4 Initial Assessment for the Environment

The release of tris(2-hydroxyethyl) isocyanurate into the environment is considered to be negligible judging from its production process and main use pattern. If the chemical is released from polymers containing it as a stabilizing agent, it will eventually be distributed into the water compartment due to its high stability in water and will persist in the water environment because of its lack of biodegradability. However, bioaccumulation of the chemical is not expected, taking into account its low BCF. Moreover, the toxicity of the chemical to aquatic organisms is low, as revealed by the acute toxicity tests to aquatic organisms (*Selenastrum capricornutum*, *Daphnia magna* and *Oryzias latipes*) and the chronic toxicity test to *Daphnia magna*.
Therefore, tris(2-hydroxyethyl) isocyanurate seems to be not hazardous to the environment.

4. HUMAN HEALTH HAZARDS

4.1 Effects on Human Health

4.1.1 Toxicokinetics and Metabolism and Mode of Action

No data were available on toxicokinetics and metabolism and mode of action for tris(2-hydroxyethyl) isocyanurate.

4.2.2 Acute Toxicity

a) Acute oral route

Two studies were available, and one of the studies was regarded as a key study for acute oral toxicity because it was well conducted in compliance with GLP and described in detail.
In this well-conducted study, four groups of rats were administered doses of 0, 500, 1,000 and 2,000 mg/kg bw of tris(2-hydroxyethyl) isocyanurate according to the OECD Test Guideline 401 (MHLW, Japan, 2001). No death occurred in any treated groups. No treatment related effect was observed in clinical signs, body weight changes and necropsy findings. The oral LD_{50} value was greater than 2,000 mg/kg bw for both male and female rats.
As supportive data, another reliable study is available, where 5 rats of each sex were administered a solution of the chemical by gavage at 10,000 mg/kg bw . No mortality and no necropsy findings were observed, and the oral LD_{50} value was suggested to be greater than 10,000 mg/kg bw for rats of both sex (BASF AG, 1976).

b) Acute inhalation route

There was one study, which was reliable, regarding acute inhalation toxicity, using rats of both sexes (BASF AG, 1976).
Three animals of each sex were exposed to the dust of tris(2-hydroxyethyl) isocyanurate at 9.32 or 15 mg/L (nominal concentration) for 8 hours. No mortality, no symptoms and no necropsy findings were revealed.

c) Acute dermal route

No data were available on acute toxicity via the dermal route.

d) Acute toxicity in other routes

There was only one study on acute toxicity in mice by intraperitoneal injection (BASF AG, 1976). In this study, five animals of each sex were injected an aqueous solution of tris(2-hydroxyethyl) isocyanurate intraperitoneally at one limited dose, 10,000 mg/kg bw, and no clinical signs, no mortality and no necropsy findings were observed. The i.p LD_{50} value was greater than 10,000 mg/kg bw for mice of each sex.

Human data:

There was no available information on humans.

Conclusions:

The LD_{50} value via oral exposure route in rats is greater than 2,000 mg/kg bw. The acute dust inhalation toxicity test for 8 hours in rat showed no symptoms and no mortality at 9.32 mg/L and 15 mg/L. Also, the LD_{50} value by intraperitoneal injection is greater than 10,000 mg/kg bw.

4.2.3 Skin Irritation

There was only one study, which was reliable but not conducted according to current standard guideline nor to GLP, on skin irritation in rabbits.
In this test, an aqueous solution of 80% tris(2-hydroxyethyl) isocyanuratewas applied to rabbits for 1, 5, 15 minutes and 20 hours, and no effects were observed 8 days after the application (BASF AG, 1976). Thus, this test revealed negative results on skin irritation on rabbits.

Human data:

There was no available information on humans.

Conclusions:

Tris(2-hydroxyethyl) isocyanurate is not irritant to skin on rabbits.

4.2.4 Eye Irritation

There was only one study, which was reliable but not conducted according to current standard guideline nor to GLP, on eye irritation in rabbits. In this study, 50 mg/animal of tris(2-hydroxyethyl) isocyanurate were applied to the eyes of rabbits and the eyes were observed at 1 hour, 24 hours and 8 days after the application. The results revealed no effects after 24 hours (BASF AG, 1976).

Human data:

There was no available information on humans.

Conclusions:

Tris(2-hydroxyethyl) isocyanurate is not irritant to eyes on rabbits.

4.2.5 Skin Sensitization

No data are available.

4.2.6 Repeated Dose Toxicity

Only one study was available on repeated dose toxicity of tris(2-hydroxyethyl) isocyanurate, and regarded as a key study since the study was well controlled and conducted according to GLP, and described in detail.
Male and female SD rats (12 animals/sex/group) were orally administered (by gavage) at doses of 0, 30, 100, 300 and 1,000 mg/kg bw/day according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] (MHLW, Japan, 2001). In male rats, the administration period was 49 days involving 2 weeks prior to mating, 2 weeks of mating and 3

weeks after the completion of the mating period. In female rats, in addition to a maximum 4 weeks pre-mating and mating period, they were treated through the pregnant period until day 3 of lactation (40-46 days in total).
No deaths or abnormalities in clinical signs were observed in any male or female animals. Also, there were no adverse effects related to the dosing of the chemical in body weights and food consumption. No treatment-related effects were found for hematological, biochemical, gross findings and organ weights. In histopathological examinations, very slight (marginally positive) extramedullary hematopoiesis in the liver was noted in only two female animals (2/12 animals) at 1,000 mg/kg bw/day. Although the author showed this change was substance-related in the original paper, it was considered not to be an adverse effect because the change was not statistically significant from the control and no other changes were observed at this dose level. Thus, the NOAEL for repeated dose toxicity in male and female rats is estimated to be 1,000 mg/kg bw/day.

Human data:

There was no available information on humans.

Conclusions:

In the OECD combined repeated dose and reproductive/developmental toxicity test, the NOAEL for repeated dose toxicity in both sexes of rats is estimated to be 1,000 mg/kg bw/day.

4.2.7 Genetic Toxicity

Bacterial tests
Three studies were available regarding reverse gene mutation. One of these studies was regarded as a key study because it was well conducted under GLP and described in detail.
In the key study, tris(2-hydroxyethyl) isocyanurate showed negative results in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 *uvr*A at concentrations up to 5,000 ug/plate with or without metabolic activation system using a pre-incubation method in line with the Guideline for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guideline 471 (MHLW, Japan, 2001). Also, no cytotoxicity was observed at the highest concentration in this study (MHLW, Japan, 2001).
Supporting negative results and no cytotoxicity were shown in the other study with *Salmonella typhimurium* TA97, TA98, TA100, TA1535, TA1537 using tris(2-hydroxyethyl) isocyanurate (at a purity of greater than 82%) as test substance at concentrations of 100 - 10,000 ug/plate with and without activation (Zeiger, E. et al., 1992).

Non-bacterial tests *in vitro*
Two chromosomal aberration tests and one sister chromatid exchange assay were available. One of the chromosomal aberration tests was well conducted under GLP and described in detail, and regarded as a key study.
The chromosomal aberration test was conducted with cultured Chinese hamster lung (CHL/IU) cells at concentrations of 653, 1,306 and 2,612 ug/mL of the chemical according to the Guideline for screening Mutagenicity Testing of Chemicals (Japan) and OECD TG 473 (MHLW, Japan, 2001). The maximum concentration with no apparent cytotoxic effect in short-term (6 hours) and continuous treatments (24 hours) was used as an upper limit.
Structural chromosomal aberrations or polyploidy were not observed up to a maximum concentration of 2,612 ug/mL under conditions of both continuous and short-term treatment with or without an exogenous metabolic activation system (MHLW, Japan, 2001).

Another *In vitro* chromosomal aberration test and a sister chromatid exchange assay were conducted with tris(2-hydroxyethyl) isocyanurate with a purity of greater than 82% (Loveday, K. et al., 1990). The chromosomal aberration test was conducted with cultured Chinese hamster ovary (CHO) cells at concentrations of 0, 402, 1,210, 4,020 ug/mL without activation and 0, 381, 1,140, 2,290, 3,810 ug/mL with activation. The sister chromatid exchange assay was conducted at concentrations of 0, 386, 1,160, 3,860 ug/mL. The highest dose used for the sister chromatid exchange assay was based on solubility or cytotoxicity, with the highest dose scored being that allowing sufficient metaphase cells for analysis at the time of harvest. Test concentrations for the chromosomal aberration test were empirically chosen based on toxicity and cell cycle delay as noted in the *in vitro* sister chromatid exchange assay. No further details on dose selection were reported. These tests revealed no cytotoxicity and negative results with and without activation.

In vivo test
No data were available on *in vivo* genotoxic effects for tris(2-hydroxyethyl) isocyanurate.

Conclusions:

Although there is no *in vivo* study, it is considered that the chemical is not genotoxic based on the negative results in some *in vitro* studies regarding bacterial mutation, chromosomal aberration and sister chromatid exchange.

4.2.8 Carcinogenicity

No data were available on carcinogenicity for the chemical.

4.2.9 Reproductive/Developmental Toxicity

There was only one study on reproductive/developmental toxicity, which was conducted according to the OECD combined repeated dose and reproductive/developmental toxicity, and identified as a key study with sufficient description.
Tris(2-hydroxyethyl) isocyanurate was studied for oral toxicity in SD rats according to OECD TG 422 at doses of 0, 30, 100, 300 and 1,000 mg/kg bw/day, as described above (section 4.2.6). Although this combined study was designed to investigate reproductive capability in parental generation as well as development in F_1 offspring, parameters to evaluate developmental toxicity were limited to only body weights at day 0 and day 4 after birth, and autopsy findings at day 4.
The chemical showed no adverse effects on copulation or fertility indexes. No changes related to the dosing of the chemical were observed in gestation length and any parameters during gestation, delivery and lactation periods. The chemical also did not show any adverse effects on the sex ratio, body weights or viability of pups. No morphological abnormalities in external and visceral observation in pups were found in any of the treated groups (MHLW, Japan, 2001).
The NOAEL for reproductive/developmental toxicity for both parents and F_1 offspring is considered to be 1,000 mg/kg bw/day.

Human data:

There was no available information on humans.

Conclusions:

The NOAEL for reproductive/developmental toxicity for both parents and F_1 offspring is considered to be 1,000 mg/kg bw/day.

4.2.10 Other Human Health Related Information

No data were available.

4.3 Initial Assessment for Human Health

No data are available on the effects to humans.
In acute oral toxicity studies, there is one key study showing that the oral LD_{50} value of tris(2-hydroxyethyl) isocyanurate for rats is greater than 2,000 mg/kg bw. The acute dust inhalation toxicity test for 8h in rat revealed no symptom and no mortality at 9.32 mg/L and 15 mg/L. Tris(2-hydroxyethyl)isocyanurate is not irritant to eye and skin on rabbits. No data are available for sensitization.
In the repeated dose toxicity as well as the reproduction and developmental toxicity, there is one key study conducted as a combined repeated dose and reproductive/developmental toxicity study in rats. There were no substance related adverse effects in any toxicological parameters. The NOAEL for repeated dose toxicity in rats is estimated to be 1,000 mg/kg bw/day.
In the above-described combined repeated dose and reproductive/developmental toxicity test in rats, the chemical showed no adverse effects on any reproductive/developmental parameters. The NOAEL for reproductive/developmental toxicity for both parents and F_1 offspring is considered to be 1,000 mg/kg bw/day.
In genetic toxicity studies, the key studies are one bacterial mutation test, and one non-bacterial *in vitro* study. The chemical was not mutagenic in bacteria and did not induce of chromosomal aberrations *in vitro*. Furthermore, supporting negative results were shown in reports concerning another *in vitro* chromosomal aberration test and an *in vitro* sister chromatid exchange assay.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1. Conclusions

5.1.1 Exposure

The production volume of tris(2-hydroxyethyl) isocyanurate in 2000 was 6,000 tonnes in Japan and 5,000 tonnes in Germany. The production and the cleaning process of the facility are conducted in a closed continuous line under remote control system.
The chemical is mainly used for synthesis of polyesters in a closed system, and thus obtained polyesters are industrially used in thermosetting varnishes and thermosetting paints for metal. It is also used in polymer industry as a stabilizer. The content in polymers is approximately 0.5% or less. One of the uses of such polymers is as exterior building material.
The chemical would not be released into the environment via wastewater from production or use sites (such as varnishes or paints industry) because organic solvents are used instead of water for the reaction media or cleaning process. Moreover, the solvent used is concentrated and then the residue of the chemical is incinerated in a well-equipped facility. As for the release from polyester products, it is considered to be negligible because most of the chemical is polymerized and it is not expected that significant quantities of monomers remain in the final polyester products. The chemical might be released from products which uses the chemical as a stabilizer. Although no data are available on the amount of the chemical used as a stabiliser, significant exposure is not expected.

Physico-chemical properties of the chemical and the Fugacity model (level III) calculation show that the chemical is likely to be distributed into water.
The half-life for photo-degradation in the atmosphere is estimated to be 13.0 h. The chemical is stable in water and not biodegradable. However, the chemical does not possess a bioaccumulation potential based on the results of a bioaccumulation test using carp (*Cyprinus carpio*). The resulting BCF was below 0.16 or 1.6 at test concentrations of 2.5 or 0.25 mg/L of, respectively.
Occupational exposure of the chemical might occur via the inhalation of dust during the packing/unpacking processes. The EHE_{inh} of dust was estimated to be 0.71 mg/kg bw/day as the worst case without any personal protection, using the EASE model. Practically, workers are obliged to use personal protection equipments (mask, glasses and gloves) during the packing/unpacking processes. Thus, the exposures to the chemical via dermal and inhalation routes are considered to be negligible.
Polymers containing the chemical as a stabilizer is the only source of the chemical which might cause consumer exposure and indirect exposure to the general population.

5.1.2 Hazards to Environment

The chemical would be distributed into the water compartment due to its high stability in water and persist in water due to its lack of biodegradability. However, bioaccumulation of the chemical is not expected because of its low measured BCF. The acute toxicity values were more than 1,000 mg/L for *Selenastrum capricornutum* (72h-NOEC, biomass and growth rate), greater than 1,000 mg/L for *Daphnia magna* (48h-EC_{50}, immobilisation) and greater than 100 mg/L for *Oryzias latipes* (96h-LC_{50}, mortality). In the chronic toxicity test with *Daphnia magna*, the 21d-NOEC (reproduction) was more than 100 mg/L. In any tests, no significant effects were observed at the concentrations tested. Therefore, tris(2-hydroxyethyl) isocyanurate seems to be non-toxic to aquatic organisms.

5.1.3 Human Health Hazard

No data are available on the effects to humans.
The acute toxicity of the chemical is low because the oral LD_{50} value in rats is greater than 2,000 mg/kg bw. Also, the acute dust inhalation toxicity test for 8h in rat revealed no symptoms and no mortality at 9.32 mg/L and 15 mg/L.
Tris(2-hydroxyethyl) isocyanurate is not irritant to eye and skin on rabbits. No data are available for sensitization.
In the combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] in rats, no deaths or abnormalities in any toxicological parameters were observed in male and female animals. The NOAEL for repeated dose toxicity in both sexes of rats is estimated to be 1,000 mg/kg bw/day. The chemical showed no adverse effects on any reproductive/developmental parameters. The NOAEL for reproductive/developmental toxicity for both parents and F_1 offspring is considered to be 1,000 mg/kg bw/day.
The chemical is considered to be not genotoxic, based on the negative results in bacterial mutation tests [OECD TG 471], an *in vitro* chromosome aberration test [OECD TG 473] and another negative *in vitro* chromosomal aberration test and sister chromatid exchange assay, which were performed according to NTP's mutagenic testing program. There is no data available from *in vivo* tests.

5.2. Recommendations

No Recommendations.
Tris(2-hydroxyethyl)isocyanurate is not a candidate for further work because all SIDS endpoints are adequately addressed and the substance has a low toxicity profile.

6. References:

BASF AG (1990a) Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date:02.11.1990)

BASF AG (1990b) Labor Oekologie; unveroeffentlichte Unter-suchung, (Ber.v.30.10.90)

BASF AG (1976) BASF Report XXV/444 (01.06.76)

BASF AG (1987) Abteilung Toxikologie; unveroeffentlichte Unter-suchung, (87/556), 06.10.87

Chemicals Evaluation and Research Institute (CERI), Japan (2001) Unpublished report.

EU (2000) International Uniform Chemical Information Data (IUCLID)

Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303.

Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report.

Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

Ministry of the Environment (MOE), Japan (2000) Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

NISSAN CHEMICAL INDUSTRIES, LTD. (2001) Unpublished report.

Zeiger, E. et al. (1992) Environ. Mol. Mutagen., 19, suppl.21, 2-141.

Appendix 1

- EHE Calculation for Occupational Exposure

.Calculation for EHE_{inh} by EASE model

EHE_{inh} = 5 mg/m^3 x 1.25 m^3/h x 8 h/day / 70kg = 0.71 mg/kg bw/day

Estimated dust level: 5 mg/m^3, exposure period: 8h/day,
Respiratory volume: 1.25 m^3/h,
Human body weight: 70 kg.

SIDS Dossier

1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-

CAS No. 839-90-7

Sponsor Country: Japan

Existing Chemical	:	ID: 839-90-7
CAS No.	:	839-90-7
EINECS Name	:	tris(2-Hydroxyethyl)-1,3,5-triazinetrione
EINECS No.	:	212-660-9
TSCA Name	:	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-
Molecular Formula	:	$C_9H_{15}N_3O_6$
Producer Related Part		
Company	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Substance Related Part		
Company	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Number of Pages	:	36

1.0.1 OECD and Company Information

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type	:	Organic
Physical status	:	Solid
Purity	:	99 % w/w
Reference	:	NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

1.1.0 DETAILS ON TEMPLATE

1.1.1 Spectra

1.2 Synonyms

1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)- (9CI)

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

1,3,5-Tris(2-hydroxyethyl) isocyanurate

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

1,3,5-Tris(2-hydroxyethyl) isocyanuric acid

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Isocyanuric acid, tris(2-hydroxyethyl) ester

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

N,N',N''-Tris(2-hydroxyethyl) isocyanurate

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

s-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)- (8CI)

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

s-Triazine-2,4,6(1H,3H,5H)-trione, tris(2-hydroxyethyl)- (6CI, 7CI)

Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

THEIC

Source	:	BASF AG Ludwigshafen

BASF Antwerpen N. V. Antwerpen 4
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Theich
Source : DEA TECH COATING S.R. ASCOLI PICENO
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Tris(.beta.-hydroxyethyl) isocyanurate
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Tris(2-hydroxyethyl) isocyanurate
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Tris(2-hydroxyethyl)-s-triazine-2,4,6-trione
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

Tris(2-hydroxyethyl) isocyanurat
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

Tris(hydroxyethyl) isocyanurate
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Reference : EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

TANAC
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

1.3 Impurities

CAS-No : 832-74-6
EINECS-No : N.A.
EINECS-Name : Bis(2-hydroxyethyl) isocyanurate
Contents : ca. 0.5 %
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

CAS-No : N.A.
EINECS-No : N.A.
EINECS-Name : 1,3-Bis(2-hydroxyethyl)-5-(2-hydroxyethyl-oxy-ethyl) isocyanurate
Contents : ca. 0.5 %
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

CAS-No : 108-80-5
EINECS-No : 203-618-0
EINECS-Name : Isocyanuric acid
Contents : Not described
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

1.4 Additives

None

1.5 Quantity

Production during the last 12 months	:	
Import during the last 12 months	:	
Quantity produced	:	6,000 tonnes at two companies in Japan and 5,000 tonnes in Germany in 2000
Reference	:	NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report) (1)
Production during the last 12 m onths	:	
Import during the last 12 months	:	
Quantity	:	10,000 – 50,000 tonnes
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

1.6.1 Labelling

None

1.6.2 Classification

None

1.7 Use Pattern

Type	:	Type
Category	:	Non dispersive use
Type	:	Type
Category	:	Use resulting in inclusion into or onto matrix
Type	:	Industrial
Category	:	Chemical industry: used in synthesis
Type	:	Industrial
Category	:	Paints and varnishes industry
Type	:	Industrial
Category	:	Stabilizer in polymers industry
Type	:	Use
Category	:	Intermediates
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

1.7.1 Technology Production/Use

No data available

1.8 Occupational Exposure Limit Values

No data available

1.9 Source of Exposure

Remarks	:	Media of release: From production site The production of the chemical and the cleaning process of its production facility are conducted in a closed continuous line under remote control.

Organic solvent is used as a reaction media or washing solvent instead of water. The solvent used is concentrated and the residue of the chemical is incinerated in a well-equipped facility. Thus, the chemical is unlikely released into environment from production site.
Although workers may be exposed to the chemical during the packing/unpacking processes, the exposure to the chemical is negligible since they are practically obliged to wear personal protection equipments, such as mask, safety glasses and gloves, and to use local ventilation equipment.

Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

Remarks : Media of release: Water from use site
The chemical is mainly used for synthesis of polyesters in a closed system, and thus obtained polyesters are used in thermosetting varnishes and thermosetting paints for metal.

: Organic solvent is used as a reaction media and the wastewater containing the chemical is not expected. Thus, the release of this chemical into water is considered to be negligible.

Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

Remarks : Media of release: From consumer products
The remaining of the chemical in products such as thermosetting varnishes or thermosetting paints for metal is not expected because the most of the chemical is polymerized under controlled polymerization reaction.
The chemical might be released from products using the chemical as a stabilizer with low content (approximately 0.5% or less). However, there are no data available on the amount of the chemical for such use in total production volume.

Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

Remarks : The organic solvent used for reaction media and cleaning process from production site is concentrated and the residue of the chemical is incinerated in a well-equipped facility.

Reference : NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)

1.14.1 Water Pollution

Classified by : Other: BASF

Labeled by : Other: BASF

Class of danger : 1 (low hazard to waters)

Remarks : Classification by Water Hazard Classes (WGK)

Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4

Reference : EU (2000) International Uniform Chemical Information Database (IUCLID) (2)

1.14.2 Major Accident Hazards

Legislation	:	Accident regulation
Substance listed	:	No
No. in directive	:	
Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	Stoerfall-Verordnung vom 20.09.1991 cited in IUCLID (2000) (3)

1.14.3 Air Pollution

Remarks	:	Not classified
Source	:	BASF AG Ludwigshafen BASF Antwerpen N. V. Antwerpen 4
Reference	:	EU (2000) International Uniform Chemical Information Database(IUCLID) (2)

1.15 Additional Remarks

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value	:	133 - 135 °C
Sublimation	:	
Method	:	Other: DIN 53 181
Year	:	
GLP	:	No data
Test substance	:	
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)

2.2 Boiling Point

Value	:	296 °C
Decomposition	:	Yes
Method	:	Other
Year	:	
GLP	:	No data
Test substance	:	
Remarks	:	Boiling point has not been acquired because of decomposition of the chemical.
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Reference	:	NISSAN CHEMICAL INDUSTRIES, LTD. (2001) Material Safety Data Sheet (MSDS) of tris(2-hydroxyethyl)-1,3,5-triazinetrione (5)
Value	:	180 °C at 4 hPa
Decomposition	:	Yes
Method	:	Other
Year	:	
GLP	:	No data
Test substance	:	
Source	:	
Reference	:	U.S. National Library of Medicine (2001) Hazardous Substances Data Bank (HSDB) (6)

2.3 Density

Type	:	Density
Value	:	1.46 g/cm^3 at 20 °C
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)
Type	:	Bulk density
Value	:	500 - 600 kg/m^3 (measured condition not described)
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)

2.3.1 Granulometry

No data available

2.4 Vapor Pressure

Value	:	0.001 Pa at 50 °C
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)
Value	:	6.1×10^{-5} Pa at 25 °C (calculated)
Method	:	Other, calculated by NOMO5
Reliabilities		(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report (7)

2.5 Partition Coefficient

Log Pow	:	-1.63 at 23 °C
Method		OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	1991
GLP	:	Not described
Test substance	:	-Source: BASF, Antwerpen. -Purity: >98%
Remarks	:	-Method After the partition equilibrium of test substance was established between n-octanol and water phase at three volume ratios, the concentrations of test substance in both phases were determined by HPLC (high performance liquid chromatography). -Result Concentration of test substance in n-octanol and water phases under three test conditions (at 23°C):

	n-octanol phase ($C_{n\text{-octanol}}$)	Water phase (C_{water})	pH	Pow ($C_{n\text{-octanol}}$ / C_{water})	Log Pow
1	0.108	4.80	7.6	0.0225	-1.65
2	0.223	10.3	7.5	0.0217	-1.66
3	0.333	13.0	7.4	0.0256	-1.59
Mean	-	-	-	0.0233	-1.63

Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Analytik; unveroeffentlichte Untersuchung (BRU 91.369 vom 26.04.1991) (8)

2.6.1 Water Solubility

Value	:	820 g/L at 20 °C
Qualitative	:	
pKa	:	
pH	:	

Remarks	:	51 g/ 100 g water at 5 °C 82 g/ 100 g water at 20 °C 169 g/ 100 g water at 40 °C 320 g/ 100 g water at 60 °C
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Reference	:	NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report (1)
Value	:	1,150 g/L at 20 °C
Qualitative	:	
pKa	:	
pH	:	7 at 100 g/L at 20 °C
Reliabilities	:	(2) Valid with restrictions
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)

2.6.2 Surface Tension

No data available

2.7 Flash Point

Value	:	270 °C
Type	:	Open cup
Method	:	Other: DIN ISO 2592
Year	:	
GLP	:	No data
Test substance	:	
Reliabilities	:	(2) Valid with restrictions
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)
Value	:	265.2 °C
Type	:	
Method	:	
Year	:	
GLP	:	No data
Test substance	:	
Reliabilities	:	(2) Valid with restrictions
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Reference	:	NISSAN CHEMICAL INDUSTRIES, LTD. (2001) Material Safety Data Sheet (MSDS) of tris(2-hydroxyethyl)-1,3,5-triazinetrione (5)

2.8 Auto Flammability

Value	:	430 °C
Method	:	Other: DIN 51 794
Year	:	
GLP	:	No data
Test substance	:	
Reliabilities	:	(2) Valid with restrictions
Source	:	BASF AG Ludwigshafen
Reference	:	BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000) (4)

2.9 Flammability

No data available

2.10 Explosive Properties

No data available

2.11 Oxidizing Properties

No data available

2.12 Additional Remarks

Type	:	Koc
Value	:	10
Method	:	Other, Calculated, PCKOCWIN v.1.66
Reliabilities	:	(2) Valid with restrictions
Reference	:	Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report (7)

3.1.1 Photodegradation

Type	:	Air
Light source	:	
Light spect.	:	
Rel. intensity	:	
Indirect photolysis		
Sensitizer	:	OH radical
Conc. of sens.	:	5 x 10^{5} molecule/cm^{3}
Rate constant	:	= 2.96 x 10^{-11} cm^{3}/(molecule x sec)
Degradation	:	= 50 % after 13.0 h
Deg. Product	:	
Method	:	Other (calculated), AOPWIN Ver.1.90
Year	:	2001
GLP	:	No
Test substance	:	
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report (7)

3.1.2 Stability in water

Type	:	Hydrolysis
Concentration	:	100 mg/L
Temperature	:	50 °C
Period	:	5 days
Method	:	OECD TG 111 (Hydrolysis as a function of pH)
Results:		Stable at pH 4, 7 and 9 (Hydrolysis was not observed in water)
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Test substance	:	-Source: Wako Pure Chemical Industries,Ltd. -Lot No. CAE1919 -Purity: 98.0 %
Reliability:		(1) Valid without restrictions
Flag:		Critical study for SIDS endpoint
Reference:		Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report (9)

3.1.3 Stability in soil

No data available

3.2 Monitoring data

No data available

3.3.1 Transport between environmental compartments

THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media	:	Air-sediment-soil-water
Method	:	Fugacity model (level III)
Results	:	

Compartment	Release : 100 % to air	Release : 100 % to water	Release : 100 % to soil
Air	0.0 %	0.0 %	0.0 %
Water	50.3 %	99.6 %	44.6 %
Soil	49.5 %	0.0 %	55.2 %
Sediment	0.2 %	0.4 %	0.2 %

Remarks: The detailed results and the input parameters used in the calculation are shown in Appendix 1, in which the calculated value by NOMO5 was used for vapor pressure instead of the measured value at 50°C.

Reliabilities : (2) Valid with restrictions
Flag : Critical study for SIDS endpoint
Reference: Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report

(7)

3.3.2 Distribution

No data available

3.4 Mode of degradation in actual use

Remarks : No data available
Source : BASF AG Ludwigshafen
Reference : EU (2000) International Uniform Chemical Information Database (IUCLID) (2)

3.5 Biodegradation

Type : Aerobic
Inoculum : Activated sludge cultivated for OECD TG 301C
Concentration : 100 mg/L related to test substance
Contact time : 14 days
Degradation : 0 % from BOD
2.5 % from TOC
7.2 % from LC
Result : Not readily biodegradable
Deg. Product : No degradation products
Method : OECD TG 301C
Thirty mg of the test substance or aniline (reference substance) and 9 mg as MLSS of activated sludge were added to 300 mL of test medium (OECD TG 301C). The test and reference solutions were cultivated in BOD meter together with the inoculum blank and abiotic control ones at 25 °C for 14 days, during which the oxygen consumption was continuously measured. After termination of the test, the residual amount of the test substance was determined with LC and TOC meter. The biodegradability was calculated from the oxygen consumption and the residual amount.
Year : 1977
GLP : No
Test substance : Purity: unknown
Source : NISSAN CHEMICAL INDUSTRIES, LTD.
Reliability : (2) Valid with restrictions
Flag : Critical study for SIDS endpoint
Reference : Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report (9)

Type	:	Aerobic
Inoculum	:	
Contact time	:	
Degradation	:	< 1 % after 5 day
Result	:	
Deg. Product	:	
Method	:	Other: BOD -Test
Year	:	
GLP	:	No data
Test substance	:	
Source	:	BASF AG Ludwigshafen
Reliability	:	(4) Not assignable because only secondary data was available
Reference	:	BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung cited in IUCLID (2000) (10)
Type	:	Aerobic
Inoculum	:	Effluent from a wastewater plant treating municipal sewage
Concentration	:	48 mg/L equivalent to 20 mg/L DOC (Dissolved Organic Carbon)
Contact time	:	28 days
Degradation	:	0 % (DOC) after 28 day
Result	:	Not readily biodegradable
Deg. Product	:	
Method	:	OECD Guide-line 301 E (1981) "Ready biodegradability: Modified OECD Screening Test"
Year	:	1990
GLP	:	Not described
Test substance	:	Other, TS
Remarks	:	- Reference substance: sodium benzoate - Degradation of reference: 100% DOC after 4 days
Source	:	BASF AG Ludwigshafen
Reliability	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date:02.11.1990) (11)
Type	:	Aerobic
Inoculum	:	Municipal activated sludge
Concentration	:	1,000 mg/L equivalent to 400 mg/L DOC (Dissolved Organic Carbon)
Contact time	:	28 days
Degradation	:	0 % (DOC) after 28 day
Result	:	Not inherently biodegradable
Deg. Product	:	
Method	:	OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year	:	1990
GLP	:	Not described
Test substance	:	Other, TS
Remarks	:	-Reference substance: diethylene glycol -Degradation of reference: 100% DOC after 7 days
Source	:	BASF AG Ludwigshafen
Reliabilities	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date: 23.10.1990) (12)

3.6 BOD_5, COD or BOD_5/COD ratio

Method	:	The biochemical oxygen demand in 5 days (BOD_5) was determined according to a German method (Deutsche Einheitsverfahren zur Wasser-Abwasser- und Schlammuntersuchung, Weinheim 1982). The chemical oxygen demand (COD) was determined according to a German standard (Deutsche Norm DIN 38409 Teil 43).
Year	:	1990
GLP	:	Not described
Concentration	:	
Inoculum	:	Effluent from BASF'S waste water treatment plant
Results	:	The test substance is not biodegradable under the test conditions.
Remarks	:	Results: -BOD_5 = 4 mg/g
Source	:	BASF AG Ludwigshafen
Reliability	:	(2) Valid with restrictions
Reference	:	BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung (Original registration No. 1901210, Date: 03.09.1990) (13)

3.7 Bioaccumulation

Species	:	*Cyprinus carpio* (carp)
Exposure period	:	42 days at 25 °C
Concentration	:	2.5 and 0.25 mg/L
BCF	:	=< 0.16 at 2.5 mg/L and =< 1.6 at 0.25 mg/L
Elimination	:	Not conducted
Method	:	OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish" Test concentration: Two exposure concentrations were set at 2.5 and 0.25 mg/L taking account of the acute toxicity value to *Oryzias latipes* (48h-LC_{50}; >1000 mg/L) in the preliminary test and the detection limit of analytical method used. Preparation of stock and test solution: The stock solution was prepared by dissolving the test substance in water. The stock solution of 200 times higher concentration than exposure concentration was diluted with dilution water in test vessel of 100 litters. Test organisms: average body weight: 23 g, average total length: 10 cm Test condition: Flow-through method at flow-rate of 400 mL/min during test period. Analysis: The concentrations of test substance were determined twice a week and three test fish was picked up every 2 weeks, two of which were subjected to analysis of concentration in test fish. Bioconcentration factor was calculated as ratio of the concentration of test substance of fish to medium.
Year	:	1978
GLP	:	No
Test substance	:	
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Reliability	:	(1) Valid without restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report (9)

3.8 Additional remarks

None

4.1 Acute/prolonged toxicity to fish

Type : Semi-static
Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 96 h
Unit : mg/L
Analytical monitoring : Yes
LC_{50} : > 100
LC_{10} : = 100
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 2000
GLP : Yes
Method : - Test organisms:
a) Size (Length and Weight): 16.4-21.1 mm in length, 0.074-0.122 g in body weight
b) Age: Not described
c) Pretreatment: Acclimated for 12 days before testing; The group showing less than 5 % mortality for 7 days before test was used.
d) Supplier/Source: Sankyo Fisheries Co. Ltd. (1-1 Ichigaya-tamachi Shinjuku-ku Tokyo, Japan)
- Test conditions:
a) Dilution water source: Dechlorinated tap water
b) Dilution water chemistry: Hardness: 60 mg/L as $CaCO_3$, pH:7.6(22°C)
c) Exposure vessel type: All glass 5-L aquaria
d) Nominal concentrations (as mg/L): 0 and 100
e) Vehicle/Solvent and concentrations: Not used
f) Stock and test solution preparation: Two g of the test substance was dissolved in 200 mL pure water to produce a 10,000 mg/L stock solution and test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
g) Number of replicates: One vessel per treatment
h) Individuals per replicates: Ten fish per replicate
i) Loading: About 0.2 g/L
j) Renewal rate of test solution: The test solution was renewed every 24 h.
k) Water temperature range: 23.3-23.7 °C
l) Light condition: 16h:8h light:darkness cycle
m) Feeding: no
- Analytical monitoring: Measured by capillary electrophoresis at the beginning of the test and after 24 h

Result : - Measured concentrations (as mg/L): <0.9 for control, 91.9 for the test solution at the beginning of the test; <0.9 for control, 92.0 for the test solution after 24 h
- Water chemistry in test (O_2, pH): DO (mg/L); 5.7-8.3, pH; 7.3-7.8
- Cumulative mortality:

Nominal Concentration	Cumulative mortality (%)			
(mg/L)	24 h	48 h	72 h	96 h
Control	0	0	0	0
100	0	0	10	10

- Abnormal response: No abnormal responses in the test solution and control during exposure
- Reference substance result: LC_{50} of copper sulfate pentahydrate at 96 h; 1.5 mg/L.

Test substance : - Source: Tokyo Kasei Kogyo Co., LTD
- Lot No. GE01
- Purity; 99.7 %

Reliability : (1) Valid without restrictions
Flag : Critical study for SIDS endpoint
Reference : Ministry of the Environment (MOE), Japan (2000). Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd. (14)

4.2 Acute toxicity to aquatic invertebrates

Type : Static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 h
Unit : mg/L
Analytical monitoring : Yes
EC_{50} : > 1,000
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year : 2000
GLP : Yes
Method : - Test organisms:
a) Age: < 24 h old
b) Pretreatment: The group of parent showing less than 5 % mortality for 14 days before test was used.
c) Species/strain/supplier: *Daphnia magna* obtained from National Institute for Environment Studies (NIES)
- Test conditions:
a) Dilution water source: Elendt M4 medium
b) Exposure vessel type: 100 mL test solution in a 100 mL glass beaker
c) Nominal concentrations (as mg/L): 0 and 1,000
d) Vehicle/solvent and concentration: Not used
e) Stock and test solution preparation: Five hundred mg of the chemical was dissolved in 500 mL dilution water to produce the stock solution of 1,000 mg/L and the test solution was prepared by adding the appropriate amount of the stock solution into the dilution water of test vessel.
f) Number of replicates: Four beakers per treatment
g) Individuals per replicates: Five daphnids per replicate
h) Renewal rate of test water: The test water was not renewed during the test.
i) Water temperature range: 20.0-21.0°C
j) Light condition: <800 lx, 16h:8h light-darkness cycle
k) Feeding: No
- Analytical monitoring: Measured by capillary electrophoresis at start of the test and after 48 h

Result : - Measured concentration (as mg/L): <1 for control, 930 for the test solution at the beginning of the test; <1 for control, 930 for the test solution at end of the test.
- Water chemistry in test (O_2, pH): DO (mg/L); 7.5-8.6, pH; 7.8-8.2
- Cumulative Immobility:

Nominal Concentration (mg/L)	Cumulative immobility (%) 24 h	48 h
Control	0	0
1,000	0	0

- Reference substance results: EC_{50} of potassium bichromate at 48 h; 0.57 mg/L

Test substance : - Source: Tokyo Kasei Kogyo Co., LTD
- Lot No. GE01

- Purity; 99.7 %

Reliability : (1) Valid without restrictions
Flag : Critical study for SIDS endpoint
Reference : Ministry of the Environment (MOE), Japan (2000) Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd. (14)

4.3 Toxicity to aquatic plants e.g. algae

Species : *Selenastrum capricornutum* (Algae)
Endpoint : Biomass
Exposure period : 72 h
Unit : mg/L
Analytical monitoring : Yes
EC_{50} : > 1000
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2000
GLP : Yes
Test condition : - Test organisms:
a) *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- Test conditions:
a) Preculture: Precultured for 4 days under the same conditions as test condition
b) Growth/test medium: OECD medium
Shaking: 100 rpm
c) Exposure vessel type: 100 mL medium in a 300 mL conical flask with a cap which allow ventilation
d) Nominal concentrations (as mg/L): 0 and 1,000 mg/L
e) Vehicle/solvent and concentration: Not used
f) Stock solutions preparation: Five hundred mg was dissolved in 50 mL pure water to produce the stock solution of 10,000 mg/L and the test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
g) Number of replicates: Triplicate per treatment
h) Initial cell number in cells/mL: $1x10^4$
i) Water temperature range: 22.3-23.1 ?
j) Light levels and quality during exposure: 4,000 lx (+/- 20 %), continuous
- Analytical monitoring: Measured by capillary electrophoresis at the beginning and end of the test.
- Statistical methods: Student t test after confirmation for homogeneity of variances by F test (because a mean value at 1,000 mg/L was compared to that of control)

Result : - Measured concentrations in mg/L: <1 for control, 954 for the test solution at the beginning of the test; <1 for control, 927 for the test solution at the end of the test
- Water chemistry in test (pH) in one replicate of each concentration (at start and end of the test): pH=7.9 at start and 9.8-9.9 at end of the test (72 h)
- Cell density at each flask at each measuring point:

Nominal Concentration (mg/L)	Mean cell densities (cells/mL) 0 h	24 h	48 h	72 h
Control	10,000 (0)	51,900 (1,900)	445,900 (47,100)	2,782,900 (85,000)
1,000	10,000 (0)	56,100 (6,600)	459,600 (30,800)	2,706,300 (105,000)

Values in parentheses show standard deviation (n=3).

- Growth curves: Percent biomass/growth rate inhibition per concentration: 1.1 % for area under growth curve (0-72 h), 2.0 % for growth rate (24-48 h), 2.5 % growth rate (24-72 h)
- Statistical results, as appropriate: Significant difference was not observed between values at 1,000 mg/L and in control
- EC_{50}/NOEC: ErC_{50} >1,000 mg/L (24-48 h); ErC_{50} >1,000 mg/L (24-72 h); EbC_{50} >1,000 mg/L (0-72 h); NOEC(r) >=1,000 mg/L (24-48 h); NOEC(r) >=1,000 mg/L(24-72 h); NOEC(b) >=1,000 mg/L(0-72 h); calculated based on nominal concentrations.
- Reference substance result: EbC_{50} of potassium bichromate at 72 h; 0.423 mg/L

Test substance : - Source: Tokyo Kasei Kogyo Co., Ltd
- Lot No. GE01
- Purity: 99.7 %

Reliability : (1) Valid without restrictions

Flag : Critical study for SIDS endpoint

Reference : Ministry of the Environment (MOE), Japan (2000) Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd. (14)

4.4 Toxicity to microorganisms e.g. bacteria

Type : Aquatic

Species : *Pseudomonas putida* (Bacteria)

Exposure period : 17 h

Analytical monitoring :

Test concentration : 0, 78.13, 156.25, 312.5, 625, 1,250, 2,500, 5,000, 10,000 mg/L

EC_{10} : > 10,000 mg/L after 17 h

EC_{50} : > 10,000 mg/L after 17 h

EC_{90} : > 10,000 mg/L after 17 h

Method : Other: German standard DIN 38412 Part 8, draft
(The Bacteria Growth inhibition Test)
The toxic effects of the test substance were determined by measuring the growth of a bacteria culture with the test substance at different concentrations and comparison to a blank without test substance.

Remarks : Test details:
- Test volume: 10 mL
- Test culture:
• Concentration of the salts and nutrients of the DIN-medium [g/L]

	Stem culture	Pre-culture	Test culture
$NaNO_3$	1.06	1.06	8.48
K_2HPO_4	0.6	0.6	4.8
KH_2PO_4	0.3	0.4	2.4
$MgSO_4 \cdot 7H_2O$	0.2	0.2	4.0
D(+)-Glucose	10.0	10.0	80.0
$FeSO_4 \cdot 7H_2O$	0.01	–	0.01
Iron citrate	–	0.06	--
Yeast extract	1.0	0.056	--

• Stem culture: Inoculation on solid agar media (weekly) at 25°C
• Pre-culture: 100 mL fluid in 300mL Erlenmeyer flasks with 1 baffle for 7 +/- 1 h at 25°C. The flasks were shaken at 150 rpm.
- Temperature: 20°C
- Shake velocity: 150 U/min
8 parts of the diluted substance (factor 1.25)
1 part of test medium

1 part of bacterial suspension (10TE/F)
- Measurements: Optical density at 436 nm after 17 h
Results:
-Optical density at 436 nm after 17 h:

Nominal Conc. (mg/L)	inoculated	uninoculated	net value	% of control.
0 (control)	0.534			
78.13	0.642	0.001	0.641	120.2
156.25	0.646	0.000	0.646	121.09
312.5	0.651	0.000	0.651	122.02
625	0.657	0.000	0.657	123.2
1,250	0.561	0.002	0.559	104.78
2,500	0.536	-0.001	0.537	100.61
5,000	0.538	-0.001	0.539	101.03
10,000	0.555	-0.001	0.556	104.22

Year : 1989
GLP : Not described
Test substance : Other, TS
Source : BASF AG Ludwigshafen
Reference : BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (No. 9/1890497, Date: 30.05.1989) (15)

Type :
Species : Activated sludge, domestic
Exposure period : 30 minute(s)
Unit : mg/L
Analytical monitoring :
EC_{10} : > 1,000
Method : Other: Test for Inhibition of Oxygen Consumption by Activated Sludge, ISO 8192
Year :
GLP : No data
Test substance :
Remarks : Disturbance of degradation by the activated sludge was not expected.
Source : BASF AG Ludwigshafen
Reference : BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Ber.v.30.10.90) cited in IUCLID (2000) (16)

4.5.1 Chronic toxicity to fish

4.5.2 Chronic toxicity to aquatic invertebrates

Type : Semi-static
Species : *Daphnia magna* (Crustacean)
Endpoint : Reproduction rate
Exposure period : 21 day
Unit : mg/L
Analytical monitoring : Yes
NOEC : >= 100
LOEC : > 100
EC_{50} : > 100
Method : OECD Guide-line 211, "*Daphnia magna* Reproduction Test"
Year : 2000
GLP : Yes
Method : - Test organisms:

Age: < 24 h old
b) Pretreatment: The group of parent showing less than 5 % mortality for 14 days before testing was used.
Species/strain/supplier: Daphnia magna obtained from National Institute for Environment Studies
- Test conditions:
a) Dilution water source: Elendt M4 medium
b) Dilution water chemistry: Hardness: 220-245 mg/L as $CaCO_3$
c) Exposure vessel type: 100 mL glass beaker
d) Nominal concentrations (as mg/L): 0 and 100
e) Vehicle/solvent and concentration: Not used
f) Stock and test solutions preparation: Five hundred mg of the test substance was dissolved in 25 mL pure water to produce 20,000 mg/L stock solution and test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
g) Number of replicates: Ten per treatment
h) Individuals per replicates: One per replicate
i) Renewal rate of test water: The test water was renewed every 48 h.
j) Test temperature range: 19.8-20.2 °C
k) Lighting: <800 lx, 16h:8h light-dark cycle
l) Feeding: *Chlorella vulgaris*, 0.15 mgC/day/individual
- Analytical procedures: Measured by capillary electrophoresis, 1 set (before and after the replacement of the test water) a week
- Statistical methods: F test and Student t-test

Result : - Measured concentrations: <1 mg/L for control, 92-97 mg/L for test solutions
- Water chemistry in test (O_2, pH): DO (mg/L); 8.2-8.9; pH; 7.2-8.4
- Cumulative numbers of dead parental Daphnia: 0 % mortality at control and 100 mg/L
- Time of the first production of young: 7 d at control and 100 mg/L
- Mean cumulative numbers of young produced per live adult:

Nominal Concentration (mg/L)	Mean cumulative numbers of young produced per live adult 14 days	21 days
Control	59	118 (8.1)
100	65	118 (11.6)

Values in parentheses show standard deviation (n=10).

- EC_{50}: >100 mg/L (21 d reproduction)
- LC_{50} for parental Daphnia (21 d): >100 mg/L
- NOEC: >=100 mg/L (21 d reproduction)
- Statistical results, as appropriate: There was no statistically significant difference between data from the control and 100 mg/L test groups.

Test substance : - Source: Tokyo Kasei Kogyo Co., Ltd
- Lot No. GE01
- Purity; 99.7 %

Reliability : (1) Valid without restrictions

Reference : Ministry of the Environment (MOE), Japan (2000) Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd. (14)

4.6.1 Toxicity to soil dwelling organisms

No data available

4.6.2 Toxicity to terrestrial plants

No data available

4.6.3 Toxicity to other Non-Mamm. terrestrial species

No data available

4.7 Biological effects monitoring

No data available

4.8 Biotransformation and kinetics

No data available

4.9 Additional remarks

None

5.1.1 Acute oral toxicity

Type	:	LD_{50}
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	Male/Female
Number of animals	:	40
Vehicle	:	Water for injection
Value	:	> 2000 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	2001
GLP	:	Yes
Result	:	No treatment related clinical sign, no death observed. Significant difference was not observed in body weight gain. No treatment related effect was observed at necropsy.
Test condition	:	- No. of animals: 5 animals/sex/group - Age at study initiation: 5 weeks old - Doses: 0, 500, 1,000, 2,000 mg/kg bw - Clinical observation: Just before administration, 30 minutes, 2, 4, 6 h after administration on the day of treatment, once a day for the other days. - Observation period: 14 days - Body weight change: Day of treatment and at 1, 3, 7, 10, 14 days after treatment. - Necropsy
Test substance	:	- Source: NISSAN CHEMICAL INDUSTRIES, LTD. - Lot No. 00915-1 - Purity: 99.0 %
Reliability	:	(1) Valid without restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865. (17)
Type	:	LD_{50}
Species	:	Rat
Strain	:	Sprague-Dawley/Gassner
Sex	:	Male/Female
Number of animals	:	5 animals/sex/dose
Vehicle	:	H_2O
Value	:	> 10,000 mg/kg bw
Method	:	Other
Year	:	1976
GLP	:	No
Result	:	- Clinical signs: diarrhea; normal weight development - There were no necropsy findings in any of the animals killed at the end of the observation period; necropsy performance by a pathologist.
Test condition	:	- Doses: one limited dose; 10,000 mg/kg bw (by gavage) - Volume administered or concentration: 20 mL/kg, 50% aqueous solution of test substance - Clinical observation: 5 times at day of treatment, afterwards daily besides weekends until necropsy. - Observation period: 14 days - Body weight change: Day of treatment and at 3, 8, 14 days after treatment. - Necropsy
Remarks	:	In a dose finding test doses of 316, 1,000 and 3,160 mg/kg bw with 2 animals per dose were used in order to establish the dose for the main study; in this range finding test no mortality occurred. Therefore 10,000 mg/kg bw for the main study was chosen.
Test substance	:	Purity: ca. 99%
Source	:	BASF AG Ludwigshafen

Reliability	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF Report XXV/444, (01.06.76) and original Lab. Raw Data. (18)

5.1.2 Acute inhalation toxicity

Type	:	Dust inhalation hazard test
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	Male/Female
Number of animals	:	3 animals/sex/group
Vehicle	:	Air
Exposure time	:	8 h, rather than 7h (OECD TG 403)
Method	:	Smyth-Carpenter, Am. Ind. Hyg . Anal. (1962) 27, 95 on which OECD TG 403, Annex 5 was based.
Year	:	1975
GLP	:	No
Result	:	No mortality and no symptoms were observed. No effect was observed in body weight change. No effect was observed at necropsy. No inhalation hazards from volatile parts/dust formation under these test conditions.
Test condition	:	- Volume administered or concentration: 200 L air/h; 9.32 and 15 mg/L nominal dust concentrations - Clinical observation: 5 times at day of treatment, afterwards daily besides weekends until necropsy. - Observation period: 7 days - Body weight change: Day of treatment and at 7 days after treatment. - Necropsy
Test substance	:	Purity: 99%
Source	:	BASF AG Ludwigshafen
Reliability	:	(2) Valid with restriction
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF Report XXV/444, (01.06.76) and original Lab. Raw Data. (18)

5.1.3 Acute dermal toxicity

5.1.4 Acute toxicity, other routes

Type	:	LD_{50}
Species	:	Mouse
Strain	:	Ivanovas
Sex	:	Male/Female
Number of animals	:	5 animals/sex
Vehicle	:	H_2O
Route of admin.	:	Intraperitoneal; injection
Exposure time	:	
Value	:	> 10,000 mg/kg bw
Method	:	Other
Year	:	1976
GLP	:	No

Result : No clinical signs and no mortality were observed.
No effect was observed in body weight change.
There were no necropsy findings in any of the animals killed at the end of the observation period; necropsy performance by a pathologist.

Test condition : - Doses: one limited dose; 10,000 mg/kg bw
- Volume administered or concentration: 20 mL/kg, 50% aqueous solution of test substance
- Clinical observation: 7 times at day of treatment, afterwards daily besides weekends until necropsy.
- Observation period: 14 days
- Body weight change: At day of treatment and 3, 8, 14 days after treatment.
- Necropsy

Remarks : In a dose finding test doses of 316; 3,160 and 10,000 mg/kg bw with 2 animals per dose were used in order to establish the dose for the main study; in this range finding test no mortality occurred. Therefore, 10,000 mg/kg bw for the main study was chosen.

Test substance : Purity; ca. 99%

Source : BASF AG Ludwigshafen

Reliability : (2) Valid with restrictions

Flag : Critical study for SIDS endpoint

Reference : BASF Report XXV/444, (01.06.76) and original Lab. Raw Data.
(18)

5.2.1 Skin irritation

Species : Rabbit/Gaukler

Concentration : 80% aqueous solution of test substance

Exposure : 0.5 mL/animal

Exposure time : 1, 5, 15 minutes and 20 hours

Number of animals : 2 animals/sex/group

Result : Not irritating
Remarks;

Exposure period	Reading after 24 hours	Reading after 8 days
1 minutes	Animal1; questionable erythema	No findings
	Animal2; no findings	
5 minutes	Animal1; questionable erythema	No findings
	Animal2; no findings	
15 minutes	Animal1; questionable erythema	No findings
	Animal2; no findings	
20 hours	Animals 1+2; questionable erythema, localized	No findings

EC classification :

Method : Other
Remarks;
Grading scale; no effect, questionable, slight, strong, very strong
Grading for erythema, edema and necrosis

Year : 1976

GLP : No

Test condition : Test concentration; 80% aqueous solution of test substance
pH; neutral
Vehicle; H_2O
Total dose; 0.5 mL/animal

Test substance : Purity; ca. 99%

Source : BASF AG Ludwigshafen

Reliability	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF Report XXV/444, (01.06.76) and original Lab. Raw Data. (18)

5.2.2 Eye irritation

Species	:	Rabbit/Gaukler
Concentration	:	
Dose	:	50 mg/animal; unchanged test substance
Exposure Time	:	
Number of animals	:	2 animals/sex
Result	:	Not irritating Remarks; Irritation score: Cornea/Iris; No findings Conjuctivae; after 1 hour: slight redness; secretion Redness/Chemosis; after 24 hours: no findings
EC classification	:	
Method	:	Other Remarks; Grading scale; no effect, questionable, slight, strong, very strong Tool used to assess score; Fluorescein
Year	:	1976
GLP	:	No
Test condition	:	- pH; neutral - Observation period; 1, 24 hours and 8 days
Remarks	:	Talcum powder was used as negative control at the other eye of the animals; at the end of the observation period (8 hours) both talcum and test substance resulted in slight redness in one animal; the other animal showed no reactions.
Test substance	:	Purity; ca.99%
Source	:	BASF AG Ludwigshafen
Reliability	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	BASF Report XXV/444, (01.06.76) and original Lab. Raw Data (18)

5.3 Sensitization

No data available

5.4 Repeated dose toxicity

Species	:	Rat
Sex	:	Male/Female
Strain	:	Sprague-Dawley
Route of admin.	:	Oral (by gavage)
Exposure period	:	Males: 49 days (14 days before mating and 35 days including 14 days for mating), Females: 40-46 days (from 14 days prior to mating to day 3 of lactation)
Frequency of treatment	:	Daily
Post obs. period	:	1 day
Doses	:	0, 30, 100, 300, 1,000 mg/kg bw/day

Control group	:	Yes, concurrent vehicle, water for injection
NOAEL	:	1,000 mg/kg bw/day
LOAEL	:	>1,000 mg/kg bw/day
Method	:	OECD Guide-line 422
Year	:	2001
GLP	:	Yes
Result	:	No changes caused by the chemical were noted regarding clinical signs, body weight, food consumption, urinalysis, hematological examination, blood chemical analysis, necropsy nor organ weights. In histopathological examination, no abnormalities related to the chemical treatment were recognized in male groups. However, extramedullary hematopoiesis in the liver was noted in two female animals (2/12 animals) at 1,000 mg/kg bw/day. Although the author showed this change was the substance-related one in the original paper, it was considered to be no adverse effect because the change was not statistically significant from control and no other changes were observed at this dose level.
Test condition	:	Age at first administration: 10 weeks old No. of animals per dose: 12 per dose group – Clinical observation performed and frequency Clinical signs: Twice daily (Just before and after administration) Body weight: Male: Twice a week, Female: Twice a week for pre-mating and mating period, 0, 7, 14, 21st day of pregnancy, 0, 4th day of lactation period. Food consumption: Male: Twice a week, Female: Twice a week for pre-mating period, 2, 9, 16, 21st day of pregnancy, 4th day of lactation period. Urinalysis: Just before the termination of administration. Volume, specific gravity, color, pH, protein, glucose, ketone bodies, occult blood, bilirubin, urobilinogen, urinary sediments – Organs examined at necropsy Macroscopic: All rats were received a full macroscopic examination with tissue collection. Organ weights: The following organs were weighed at necropsy. Brain, pituitary, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries were recorded. Microscopic: The following organs were microscopically observed for control and 1,000 mg/kg bw/day group. Liver and spleen (male only) were also observed for 30, 100 and 300 mg/kg bw/day group. Brain, pituitary gland, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries, lung, trachea, pancreas, salivary glands, esophagus, stomach, duodenum, jejunum, ileum, cecum, rectum, colon, lymph node, bladder, uterus, vagina, parathyroids, spinal cord, sciatic nerve, eyes, Harderian glands, mammary gland, bone marrow, seminal vesicle, prostate – Hematology red blood cell count, white blood cell count, platelet count, hemoglobin concentration, hematocrit value, differential leukocyte count, reticulocyte count, protrombin time, activated partial thromboplastin time, fibrinogen, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration – Clinical chemistry total protein, glucose, total cholesterol, blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, total bilirubin, triglyceride, albumin-globulin ratio, albumin, sodium, potassium, calcium, inorganic phosphorus, chloride – General remarks: This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Therefore, hematological and blood chemical examinations, and urinalysis for females were not performed.
Test substance	:	- Source: NISSAN CHEMICAL INDUSTRIES, LTD. - Lot No. 00915-1

- Purity: 99.0 %

Conclusion : Male NOAEL=1,000 mg/kg bw/day
Female NOAEL=1,000 mg/kg bw/day
Reliability : (1) Valid without restrictions
Flag : Critical study for SIDS endpoint
Reference : Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.
(17)

5.5 Genetic toxicity 'in vitro'

Type : Ames test
System of testing : *Salmonella typhimurium* TA100, TA1535, TA98, TA1537, *E. coli* WP2 uvrA
Concentration : 0, 156, 313, 625, 1,250, 2,500, 5,000 ug/plate
Cytotoxic conc. : Not observed
Metabolic activation : With and without
Result : Negative
Year : 2001
GLP : Yes
Method : OECD Guideline 471 "Bacterial Reverse Mutation Test" and Screening Mutagenicity Testing of Chemicals (Japan)
Result : No increases in revertant colonies were observed in the test with either the non-activation method (-S9) or activation method (+S9).
Test condition : Plates/test: 3
Number of replicates: 2
Positive and Negative control groups and treatment: yes,
Positive controls:
-S9 mix; 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (TA100, TA98, WP2 uvrA), Sodium azide (TA1535) and 9-Aminoacridine hydrochloride (TA1537)
+S9 mix; 2-Aminoanthracene (all strains)
Solvent: Water for injection
Metabolic activation: S9mix from Phenobarbital and 5,6-benzoflavone induced rat liver microsomes.
Criteria of evaluating results: The result was designated "mutagenic" when at least two-fold increase over the control, and dose response-trend or reproducibility was observed.
Test substance : - Source: NISSAN CHEMICAL INDUSTRIES, LTD.
- Lot No. 00915-1
- Purity: 99.0 %
Reliability : (1) Valid without restrictions
Flag : Critical study for SIDS endpoint
Reference : Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.
(17)

Type : Ames test
System of testing : *Salmonella typhimurium* TA97, TA98, TA100, TA1535, TA1537
Concentration : 0, 100, 333, 1,000, 3,333, 10,000 ug/plate
Cytotoxic conc. : Not observed
Metabolic activation : With and without
Result : Negative
Method : Other
Year : 1992
GLP : No data
Method : According to the method of
Howorth, S. et al.; Environ. Mutagen., 5, suppl.1, 3-142 (1983)
Remarks : The chemical was tested within the NTP's mutagenicity testing program.
Test condition : Plates/test: 3

		Number of replicates: 2 Positive and Negative control groups and treatment: yes Positive controls: -S9 mix; 4-nitro-o-phenylenediamine (TA98, TA1538), Sodium azide (TA1535, TA100), and 9-Aminoacridine hydrochloride (TA97, TA1537) +S9 mix; 2-Aminoanthracene (all strains) Solvent: water Metabolic activation: S9mix from Aroclor 1254 induced rat and Syrian hamster liver microsomes. (10 % and 30 %) Criteria of evaluating results: Individual trials were judged to be mutagenic depending on magnitude of the increase in his+ revertants and shape of the dose-response. It was not necessary for a response to reach two-fold over background for a trial to be judged mutagenic.
Test substance	:	-Source: Tokyo-Kasei -Purity > 82 %
Reliability	:	(2) Valid with restrictions
Reference	:	Zeiger, E. et al. (1992) Environ. Mol. Mutagen., 19, Suppl.21, 2-141. (19)
Type	:	Ames test
System of testing	:	*Salmonella typhimurium* TA1535, TA100, TA1537, TA98
Concentration	:	20 – 5,000 ug/plate
Cytotoxic conc.	:	Not described
Metabolic activation	:	With and without
Result	:	Negative
Method	:	OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year	:	1983
GLP	:	No
Test substance	:	Other TS
Source	:	BASF AG Ludwigshafen
Reliability	:	(4) Not assignable because only secondary data was available
Flag	:	Non confidential
Reference	:	BASF AG; Abteilung Toxikologie; Unveroeffentlichte Untersuchung (87/556), 06.10.87 cited in IUCLID (2000) (20)
Type	:	Chromosomal aberration test
System of testing	:	Chinese Hamster Lung cells (CHL/IU)
Concentration	:	0, 653, 1,306, 2,612 ug/mL for short-term treatment (6 h) 0, 653, 1,306, 2,612 ug/mL for -S9 continuous treatment (24 h)
Cytotoxic conc.	:	Not observed
Metabolic activation	:	With and without (short-term treatment), without (continuous treatment)
Result	:	Negative
Method	:	Other
Year	:	2001
GLP	:	Yes
Method	:	OECD Guideline 4 73 "In vitro Mammalian Chromosome Aberration Test" and Screening Mutagenicity Testing of Chemicals (Japan)
Result	:	No increase in chromosomal aberrations was observed in the test with either the short-term treatment (-S9 and +S9) or continuous treatment (-S9).
Test condition	:	Positive and negative control groups and treatment: yes Positive controls: -S9 mix; Mitomycin C +S9 mix; Cyclophosphamide Solvent: Physiological saline Plate/concentration: 2 Criteria of evaluating results: The results were considered to be negative if the incidence was less than 4.9 %, equivocal if it was between 5.0 and 9.9 %, and positive if it was more than 10.0 %
Test substance	:	- Source: NISSAN CHEMICAL INDUSTRIES, LTD. - Lot No. 00915-1 - Purity: 99.0 %
Reliability	:	(1) Valid without restrictions
Flag	:	Critical study for SIDS endpoint

Reference	:	Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865. (17)
Type	:	Chromosomal aberration test
System of testing	:	Chinese Hamster Ovary cells (CHO)
Concentration	:	0, 381, 1,140, 2,290, 3,810 ug/mL for +S9 condition, 0, 402, 1,210, 4,020 ug/mL for -S9 condition
Cytotoxic conc.	:	Not observed
Metabolic activation	:	With and without
Result	:	Negative
Method	:	Other
Year	:	1990
GLP	:	No data
Method	:	Treatment period:8h(-S9) or 2h(+S9) Harvest time:10.5h(-S9) or 12h(+S9) from the beginning of the treatment
Remarks	:	The chemical was tested within the NTP's mutagenic testing program.
Test condition	:	Positive and negative control groups and treatment: yes Positive controls: -S9 mix; Mitomycin C +S9 mix; Cyclophosphamide Solvent: water Metabolic activation: S9mix from Aroclor 1254-induced rat liver microsomes. Criteria of evaluating results: The total percent cells with aberrations (simple, complex, other) were analyzed, and the positive response was defined as the case for which the P value, adjusted by Dunnett's method, was < 0.05.
Test substance	:	-Source: Tokyo-Kasei -Purity > 82 %
Reliability	:	(2) Valid with restrictions
Reference	:	Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303. (21)
Type	:	Cytogenetic assay
System of testing	:	CHO-Zellen
Concentration	:	
Cytotoxic conc.	:	
Metabolic activation	:	With and without
Result	:	Negative
Method	:	
Year	:	
GLP	:	No data
Test substance	:	Other TS
Source	:	BASF AG Ludwigshafen
Reliability	:	(4) Not assignable because only secondary data was available
Reference	:	National Toxicology Program (1987) Annual Plan for Fiscal Year, cited in IUCLID (2000) (22)
Type	:	Sister chromatid exchange assay
System of testing	:	Chinese Hamster Ovary Cells (CHO)
Concentration	:	0, 386, 1,160, 3,860 ug/mL
Cytotoxic conc.	:	Not observed
Metabolic activation	:	With and without
Result	:	Negative
Method	:	Other
Year	:	1990
GLP	:	No data
Method	:	Treatment period: 2h BrdU addition: 24h BrdU and Colcemid: 2-2.5h
Remarks	:	The chemical was tested within the NTP's mutagenic testing program.
Test condition	:	Positive and negative control groups and treatment: yes Positive controls: -S9 mix; Mitomycin C +S9 mix; Cyclophosphamide Solvent: water Metabolic activation: S9mix from Aroclor 1254-induced rat liver microsomes. Criteria of evaluating results: A trend test of the SCEs per chromosome vs. the

		log of the concentration was used. If at least two doses showed increases of at least 20 % over the control, the result was designated "+".
Test substance	:	-Source: Tokyo-Kasei -Purity > 82 %
Source	:	NISSAN CHEMICAL INDUSTRIES, LTD.
Reliability	:	(2) Valid with restrictions
Reference	:	Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303. (21)
Type	:	Sister chromatid exchange assay
System of testing	:	CHO-Zellen
Concentration	:	
Cytotoxic conc.	:	
Metabolic activation	:	With and without
Result	:	Negative
Method	:	
Year	:	
GLP	:	No data
Test substance	:	Other TS
Source	:	BASF AG Ludwigshafen
Reliability	:	(4) Not assignable because only secondary data was available
Reference	:	National Toxicology Program (1987) Annual Plan for Fiscal Year, cited in IUCLID (2000) (22)

5.6 Genetic toxicity 'in vivo'

No data available

5.7 Carcinogenity

No data available

5.8 Toxicity to reproduction

Type	:	Fertility
Species	:	Rat
Sex	:	Male/Female
Strain	:	Sprague-Dawley
Route of admin.	:	Oral (by gavage)
Exposure period	:	Males: 49days (14 days before mating and 35 days including 14 days for mating), Females: 40-46 days (from 14 days prior to mating to day 3 of lactation)
Frequency of treatment	:	Daily
Premating exposure period		
Male	:	14 days
Female	:	14 days
Duration of test	:	Until the 4th day of lactation.
Doses	:	0, 30, 100, 300, 1,000 mg/kg bw/day
Control group	:	Yes, concurrent vehicle, water for injection
NOAEL Parental	:	1,000 mg/kg bw/day
NOAEL F1 Offspr.	:	1,000 mg/kg bw/day
Method	:	Other: OECD Guide-line 422

Year	:	2001
GLP	:	Yes
Result	:	No treatment related effect was noted in the copulation index, gestation length, delivery conditions, nursing conditions, fertility index, number of corpora lutea, implantation rate nor gestation index. Regarding the pups, no abnormal findings caused by the chemical were noted in terms of the numbers of pups, stillbirths and live pups born, sex ratio, delivery index, birth index, live birth index, viability index or body weight.
Test condition	:	Age at first administration: 10 weeks old No. of animals per dose: 12 per dose group – Clinical observation performed and frequency Clinical signs: Twice daily (Just before and after administration) Estrus cycle: From the beginning of administration period to confirmed copulation. Mating: One male to one female mating until the day of confirmed copulation, for maximum 14 days. Every morning the females were examined for the presence of vaginal plug or sperm in the vaginal smear. Day 0 of pregnancy was defined as the day a vaginal plug or sperm was found. Gestation length: The duration of gestation was calculated from day 0 of pregnancy and recorded. Litters: number (0, 4th day), sex (0, 4th day), live births (0, 4th day), stillbirths (0 day), gross abnormalities (0 day). Body weight (pup): 0, 4th day after birth Necropsy: 4th day after birth Remarks: Age at study initiation was 8 weeks old for both sexes. Males were killed on the day after the administration period. Females were sacrificed on the day 4 of lactation. Females with no delivery were killed 4 days after the delivery expected date. Females showing no-evidence of copulation were sacrificed at the termination of the mating period.
Test substance	:	- Source: NISSAN CHEMICAL INDUSTRIES, LTD. - Lot No. 00915-1 - Purity: 99.0 %
Reliability	:	(1) Valid without restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865. (17)

5.9 Developmental toxicity/teratogenicity

Species	:	Rat
Sex	:	Male/Female
Strain	:	Sprague-Dawley
Route of admin.	:	Oral (by gavage)
Exposure period	:	Males: 49days (14 days before mating and 35 days including 14 days for mating), Females: 40-46 days (from 14 days prior to mating to day 3 of lactation)
Frequency of treatment	:	Daily
Duration of test	:	Until the 4th day of lactation.
Doses	:	0, 30, 100, 300, 1,000 mg/kg bw/day
Control group	:	Yes, concurrent vehicle
NOAEL Maternal.	:	1,000 mg/kg bw/day
NOAEL Teratogen	:	1,000 mg/kg bw/day
Method	:	OECD Guide-line 422
Year	:	2001
GLP	:	Yes
Result	:	Proboscis was observed in a stillbirth pup at 300 mg/kg bw/day. No treatment-related external abnormalities were observed among newborns.

Test condition	:	Age at the first administration: 10 weeks old No. of animals per dose: 12 per dose group – Clinical observation performed and frequency Clinical signs: Twice daily(Just before and after the administration) Estrus cycle: From the beginning of administration period to the day of confirmed copulation. Mating: One male to one female mating until the day of confirmed copulation, for maximum 14 days. Every morning the females were examined for the presence of vaginal plug or sperm in the vaginal smear. Day 0 of pregnancy is defined as the day a vaginal plug or sperm is found. Gestation length: The duration of gestation was calculated from day 0 of pregnancy and recorded. Litters: number (0, 4th day), sex (0, 4th day), live births (0, 4th day), stillbirths (0 day), external abnormalities (0 day). Body weight (pup): 0, 4th day after birth Necropsy: 4th day after birth
Test substance	:	- Source: NISSAN CHEMICAL INDUSTRIES, LTD. - Lot No. 00915-1 - Purity: 99.0 %
Reliability	:	(1) Valid without restrictions
Flag	:	Critical study for SIDS endpoint
Reference	:	Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865. (17)

5.10 Other relevant information

5.11 Experience with human exposure

Remarks	:	No data available
Source	:	BASF AG Ludwigshafen
Reference	:	EU (2000) International Uniform Chemical Information Data base (IUCLID) (2)

(1) NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report

(2) EU (2000) International Uniform Chemical Information Database (IUCLID)

(3) Stoerfall-Verordnung vom 20.09.1991 cited in IUCLID (2000)

(4) BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurat (13.04.1994) cited in IUCLID (2000)

(5) NISSAN CHEMICAL INDUSTRIES, LTD. (2001) Material Safety Data Sheet (MSDS) of tris(2-hydroxyethyl)-1,3,5-triazinetrione

(6) U.S. National Library of Medicine (2001) Hazardous Substances Data Bank (HSDB)

(7) Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report

(8) BASF AG, Analytik; unveroeffentlichte Untersuchung (BRU 91.369 vom 26.04.1991)

(9) Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report

(10) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung cited in IUCLID (2000)

(11) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date: 02.11.1990)

(12) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date: 23.10.1990)

(13) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung (Original registration No. 1901210, Date: 03.09.1990)

(14) Ministry of the Environment (MOE), Japan(2000) Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

(15) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (No. 9/1890497, Date: 30. 05. 1989)

(16) BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Ber.v.30.10.90) cited in IUCLID (2000)

(17) Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

(18) BASF Report XXV/444, 01.06.76

(19) Zeiger, E. et al. (1992) Environ. Mol. Mutagen., 19, suppl.21, 2-141.

(20) BASF AG; Abteilung Toxikologie; Unveroeffentlichte Untersuchung (87/556), 06.10.87 cited in IUCLID (2000)

(21) Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303.

(22) National Toxicology Program(1987) Annual Plan for Fiscal Year, cited in IUCLID (2000)

Appendix 1 Results of the calculation of the theoretical distribution

Tris(2-Hydroxyethyl)-1,3,5-triazinetrione

Scenario 1

	Emission rate	Conc.	Amount	Percent	Transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	Reaction	Advection
Air	1,000	9.2.E-12	9.2.E-02	0.0	4.9E-03	9.2.E-04
Water	0	4.7.E-02	9.5.E+05	50.3	2.7E+01	9.5.E+02
Soil	0	5.8.E-01	9.3.E+05	49.5	2.7E+01	
Sediment		3.7.E-02	3.7.E+03	0.2	3.6E-02	7.5.E-02
		Total amount	1.9.E+06			

Scenario 2

	Emission rate	Conc.	Amount	Percent	Transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	Reaction	Advection
Air	0	4.8.E-29	4.8.E-19	0.0	2.6.E-20	4.8.E-21
Water	1,000	4.9.E-02	9.7.E+05	99.6	2.8.E+01	9.7.E+02
Soil	0	3.1.E-18	4.9.E-12	0.0	1.4.E-16	
Sediment		3.8.E-02	3.8.E+03	0.4	3.7.E-02	7.7.E-02
		Total amount	9.8.E+05			

Scenario 3

	Emission rate	Conc.	Amount	Percent	Transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	Reaction	Advection
Air	0	9.7.E-27	9.7.E-17	0.0	5.1.E-18	9.7.E-19
Water	0	4.7.E-02	9.4.E+05	44.6	2.7.E+01	9.4.E+02
Soil	1,000	7.3.E-01	1.2.E+06	55.2	3.4.E+01	
Sediment		3.7.E-02	3.7.E+03	0.2	3.6.E-02	7.4.E-02
		Total amount	2.1.E+06			

Scenario 4

	Emission rate	Conc.	Amount	Percent	Transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	Reaction	Advection
Air	600	5.5.E-12	5.5.E-02	0.0	2.9.E-03	5.5.E-04
Water	300	4.8.E-02	9.5.E+05	58.4	2.8.E+01	9.5.E+02
Soil	100	4.2.E-01	6.7.E+05	41.3	1.9.E+01	
Sediment		3.8.E-02	3.8.E+03	0.2	3.6.E-02	7.5.E-02
		Total amount	1.6.E+06			

Appendix 1 (continued)

Physico-chemical parameters used

Molecular weight		261.23	Measured
Melting point [°C]		134	Measured
Vapor pressure [Pa]		6.1E-5	Calculated
Water solubility [g/m^3]		820,000	Measured
Log Kow		-1.63	Measured
Half life [h]	In air	13.005	Estimated
	In water	24,000	Estimated
	In soil	24,000	Estimated
	In sediment	72,000	Estimated

Temp. [°C]	25

Environmental parameters used

		Volume	Depth	Area	Organic	Lipid content	Density	Residence
		[m^3]	[m]	[m^2]	Carbon [-]	[-]	[kg/m^3]	time [h]
Bulk air	Air	1.0E+13					1.2	100
	Particles	2.0E+03						
	Total	1.0E+13	1,000	1E+10				
Bulk water	Water	2.0E+10					1,000	1,000
	Particles	1.0E+06			0.04		1,500	
	Fish	2.0E+05				0.05	1,000	
	Total	2.0E+10	10	2E+09				
Bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1,000	
	Solid	8.0E+08			0.04		2,400	
	Total	1.6E+09	0.2	8E+09				
Bulk sediment	Water	8.0E+07					1,000	
	Solid	2.0E+07			0.06		2,400	50,000
	Total	1.0E+08	0.05	2E+09				

Intermedia Transport Parameters [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 (xii)	0.02	Soil water runoff	5E-05
Soil water phase diffusion MTC	1E-05	Soil solid runoff	1E-08

Database Searched in 2001

No.	Database	Key word	Hit
1	ChemFinder	839-90-7	1
2	Registry	839-90-7	1
3	Beilstein	839-90-7	1
4	HSDB	839-90-7	1
5	MSDS-OHS	839-90-7	1
6	NIOSHTIC	839-90-7	1
7	Chemical Abstract	839-90-7 and toxicology/cc,sx	3
8	Toxline	839-90-7	2
9	NTP (National Toxicology Program)	839-90-7	1
10	IUCLID	839-90-7	1
11	Merck Index	839-90-7	1
12	http://wwwdb.mhlw.go.jp/ginc/html/db1-j.html (in Japanese) http://wwwdb.mhlw.go.jp/ginc/html/db1.html (in English)	839-90-7	1
13	http://www.ceri.jp/ceri_jp/koukai/koukai_menu.html (in Japanese) http://www.ceri.jp/ceri_en/koukai/koukai_menu.html (in English)	839-90-7	1
14	ATSDR	839-90-7	0
15	TSCATS	839-90-7	0
16	US IRIS	839-90-7	0
17	GENETOX	839-90-7	0
18	CCRIS	839-90-7	0
19	ACGIH	839-90-7	0
20	IARC	839-90-7	0
21	US EPA ECOTOX [AQUIRE]	839-90-7	0
22	IPCS INCHEM	839-90-7	0
23	RTECS	839-90-7	1

ROBUST STUDY SUMMARIES

for

1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2-hydroxyethyl)-

CAS No. 839-90-7

Sponsor country: Japan

OECD SIDS PHYSICAL/CHEMICAL ENDPOINTS

Melting Point

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source is not specified.

METHOD

- **Method:** DIN 53 181
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:**

RESULTS

- **Melting point value:** 133-135 °C
- **Decomposition:** Not stated
- **Sublimation:** Not stated
- **Remarks:**

CONCLUSIONS Melting point is 133-135 °C.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:**

REFERENCES BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurate (13.04.1994)

OTHER

- **Last changed**
- **Order number for sorting**
- **Remarks:**

Boiling Point

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source is not specified.

METHOD

- **Method:** Not specified
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:**

RESULTS

- **Boiling point value:** Not applicable
- **Pressure:**
- **Pressure unit:**
- **Decomposition:** At 296°C
- **Remarks:**

CONCLUSIONS Boiling point has not been acquired because of decomposition of the chemical.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:**

REFERENCES NISSAN CHEMICAL INDUSTRIES, LTD. (2001) Material Safety Data Sheet (MSDS) of tris(2-hydroxyethyl)-1,3,5-triazinetrione

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Density

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source is not specified.

METHOD

- **Method:** Not specified
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:**

RESULTS

- **Density:** 1.46 g/cm^3 (at 20 °C)
- **Remarks:**

CONCLUSIONS The density at 20 °C is 1.46 g/cm^3.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:**

REFERENCES

BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurate (13.04.1994)

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Vapor Pressure

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7))
- **Remarks:** Source is not specified.

METHOD

- **Method:** Not specified
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:**

RESULTS

- **Vapor Pressure value:** 0.001 Pa at 50 °C
- **Decomposition:** Not stated
- **Remarks:**

CONCLUSIONS The vapor pressure at 50 °C is 0.001 Pa.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:**

REFERENCES BASF AG, Sicherheitsdatenblatt Trishydroxyethylisocyanurate (13.04.1994)

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Vapor Pressure

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Method:** Calculation by MONO5
- **GLP:** No
- **Year:** 2001
- **Remarks:**

RESULTS

- **Vapor Pressure value:** 6.1×10^{-5} Pa at 25°C
- **Decomposition:**
- **Remarks:**

CONCLUSIONS The vapor pressure at 25°C is calculated as 6.1×10^{-5} Pa.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Accepted calculation method

REFERENCES Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Partition Coefficient

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: BASF, Antwerpen, Purity: >98%

METHOD

- **Method:** OECD TG 107 (Flask-shaking method)
- **GLP:** Not stated
- **Year:** 1991
- **Remarks:** After the partition equilibrium of test substance was established between n-octanol and water phases at three volume ratios, the concentrations of test substance in both phases were determined by HPLC (high performance liquid chromatography).

RESULTS

- **Log P_{ow}:** -1.63
- **Temperature:** 23 °C
- **Remarks:**

Concentration of tris(2-hydroxyethyl) isocyanurate in n-octanol and water phases under three conditions (g/L):

	n-octanol phase ($C_{n\text{-}octanol}$)	Water phase (C_{water})	pH	P_{ow} ($C_{n\text{-}octanol}/C_{water}$)	Log P_{ow}
1	0.108	4.80	7.6	0.0225	-1.65
2	0.223	10.3	7.5	0.0217	-1.66
3	0.333	13.0	7.4	0.0256	-1.59
Mean				0.0233	-1.63

CONCLUSIONS Log P_{ow} is -1.63 at 23°C.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Guideline study; basic data given

REFERENCES BASF AG, Analytik; unveroeffentlichte Untersuchung (BRU 91.369 vom 26.04.1991)

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Water Solubility

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source is not specified.

METHOD

- **Method:** Not specified
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:**

RESULTS

- **Value:** 820 g/L at 20°C
- **Description of solubility:** Very soluble
- **pH value:** Not stated
- **pKa value:** Not stated
- **Remarks:** 51 g/ 100 g water at 5°C
  82 g/ 100 g water at 20°C
  169 g/ 100 g water at 40°C
  320 g/ 100 g water at 60°C

CONCLUSIONS Water solubility is 820 g/L at 20°C.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:**

REFERENCES NISSAN CHEMICAL INDUSTRIES, LTD. Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

OECD SIDS Environmental Fate Endpoints

Photodegradation

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Method:** Calculation by AOP Win v1.90 (Environmental Protection Agency)
- **Type:** Indirect photodegradation
- **GLP:** No
- **Year:** 2001
- **Type of Sensitizer:** OH radical
- **Concentration of Sensitizer:** 5×10^5 molecule/cm^3
- **Remarks:** The rate constant for gas-phase reaction between photochemically produced hydroxyl radicals and the test substance in atmosphere was calculated by AOP Win ver. 1.90, which was 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 5×10^5 molecule/cm^3 in atmosphere.

RESULTS

- **Rate Constant:** 2.96×10^{-11} cm^3/(molecule · sec)
- **Degradation:** 50 % after 13.0 h
- **Remarks:**

CONCLUSIONS The half-life time of tris(2-hydroxyethyl) isocyanurate by the reaction with photochemically produced OH radicals in air is 13.0 h.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Accepted calculation method

REFERENCES Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report

OTHER

- **Last changed**
- **Order number for sorting**
- **Remarks:**

Stability in water

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Wako Pure Chemical Industries, Ltd., Lot No. CAE1919, Purity: 98.0 %

METHOD

- **Method/guideline:** OECD TG 111
- **Type:** Hydrolysis as a function of pH
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:** The test was performed at 100 mg/L at 50 °C for 5 days in each buffer of pH 4.0, 7.0 and 9.0.

RESULTS

- **Nominal concentration:** 100 mg/L
- **Measured value:** Not stated
- **Degradation %:** Hydrolysis was not observed.
- **Breakdown products:**
- **Remarks:**

CONCLUSIONS The substance is stable at pH 4.0, 7.0 and 9.0.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks:** Well conducted guideline study

REFERENCES Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Transport between Environmental Compartments (Fugacity)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Test (test type):** Calculation
- **Method:** Fugacity model (level III)
- **Year:** 2001
- **Remarks:**

RESULTS

- **Media:** Air, water, soil and sediment
- **Estimated Distribution and Media Concentration under three emission scenarios:**

Compartment	Release 100 % to air	Release 100 % to water	Release 100 % to soil
Air	0.0 %	0.0 %	0.0 %
Water	50.3 %	99.6 %	44.6 %
Soil	49.5 %	0.0 %	55.2 %
Sediment	0.2 %	0.4 %	0.2 %

- **Remarks:** The parameters used in the fugacity calculation are shown in Appendix 1, in which the calculated value by NOMO5 was used for vapor pressure instead of the measured value at 50 °C.

CONCLUSIONS If tris(2-hydroxyethyl) isocyanurate is released into water, the majority of substance is likely to remain in water, and if released into air or soil, almost equal amount of the substance is likely distributed into water and soil.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Accepted calculation method

REFERENCES Chemicals Evaluation and Research Institute (CERI), Japan (2001). Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Appendix 1 The parameters used in the fugacity calculation.

Physicochemical parameters used

Molecular weight		261.23	Measured
Melting point [°C]		134	Measured
Vapor pressure [Pa]		6.1E-5	Calculated
Water solubility [g/m^3]		820,000	Measured
Log Kow		-1.63	Measured
Half life [h]	in air	13.005	Estimated
	in water	24,000	Estimated
	in soil	24,000	Estimated
	in sediment	72,000	Estimated

Temp. [°C]	25

Environmental parameters used

		Volume	Depth	Area	Organic	Lipid content	Density	Residence
		[m^3]	[m]	[m^2]	Carbon [-]	[-]	[kg/m^3]	Time [h]
Bulk air	Air	1.0E+13					1.2	100
	Particles	2.0E+03						
	Total	1.0E+13	1,000	1E+10				
Bulk water	Water	2.0E+10					1,000	1,000
	Particles	1.0E+06			0.04		1,500	
	Fish	2.0E+05				0.05	1,000	
	Total	2.0E+10	10	2E+09				
Bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1,000	
	Solid	8.0E+08			0.04		2,400	
	Total	1.6E+09	0.2	8E+09				
Bulk sediment	Water	8.0E+07					1,000	
	Solid	2.0E+07			0.06		2,400	50,000
	Total	1.0E+08	0.05	2E+09				

Intermedia Transport Parameters

	[m/h]		[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

Biodegradation

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Purity: not stated

METHOD

- **Method/guideline:** OECD TG 301C
- **Test Type:** Aerobic
- **GLP:** No
- **Year:** 1977
- **Contact time:** 14 days
- **Inoculum:** Activated sludge cultivated for OECD TG 301C
- **Remarks:** Thirty mg of the test substance or aniline (reference substance) and 9 mg as MLSS of activated sludge were added to 300 mL of test medium (OECD TG 301C). The test and reference solutions were cultivated in BOD meter together with the inoculum blank and abiotic control ones at 25°C for 14 days, during which the oxygen consumption was continuously measured. After termination of the test, the residual amount of the test substance was determined with LC and TOC meter. The biodegradability was calculated from the oxygen consumption and the residual amount.

RESULTS

- **Degradation after 14 days:** 0 % from BOD
  2.5 % from TOC
  7.2 % from LC
- **Results:** Not readily biodegradable
- **Kinetic:** Not stated
- **Breakdown products:** No degradation product
- **Remarks**

CONCLUSIONS Tris(2-hydroxyethyl) isocyanurate is not readily biodegradable.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Guideline study, essential test conditions available

REFERENCES Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Biodegradation

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Method/guideline:** The modified OECD screening test: OECD Guideline for Testing of chemicals 301E (1981)
- **Test Type:** Aerobic
- **GLP:** Not stated
- **Year:** 1990
- **Contact time:** 28 days
- **Inoculum:** Effluent from a wastewater plant treating municipal sewage
- **Remarks field for Test Conditions:**

  Test details:

  - Test concentration: 48 mg/L equivalent to 20 mg/L DOC

  - Reference substance: Sodium benzoate was used as a reference substance.

Test Assay	1	2	3	4	5	6
	Blank	RS	IC	PC	TS1	TS2
TS (mg/L)			48	48	48	48
TS (mg DOC/L)			20	20	20	20
RS (mg DOC/L)		20	20			
Water (mL)	500	500	500	500	500	500
Medium (mL)	6	6	6	6	6	6
Inoculum (mL)	0.5	0.5	0.5	0	0.5	0.5
Inoculum (mg dw/L)						
Mercury chloride (mL)				1		
Stock solution TS (mL)	0	0	48.1	48.1	48.1	48.1
Stock solution RS (mL)	0	32.9	32.9	0	0	0
Rest of water (mL)	493.5	460.6	412.5	444.9	445.4	445.4
Liquid volume (mL)	1,000	1,000	1,000	1,000	1,000	1,000

RS=reference substance, IC=inhibition control,
PC=physico-chemical elimination control, TS=test substance.

RESULTS

- **Degradation:** 0% by DOC after 28 days
- **Elimination:** 0% by DOC after 28 days
- **Results:** Not readily biodegradable
- **Remarks** Degradation of reference substance: 100% DOC after 4 days

CONCLUSIONS Tris(2-hydroxyethyl) isocyanurate is not readily biodegradable.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Guideline study, essential test conditions available

REFERENCES BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date:02.11.1990)

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

Biodegradation

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Method/guideline:** OECD TG 302B by DOC analysis
- **Test Type:** Aerobic
- **GLP:** Not described
- **Year:** 1990
- **Contact time:** 28 days
- **Inoculum:** Municipal activated sludge
- **Remarks field for Test Conditions:**

Test details:

- Test concentration: 1,000 mg/L equivalent to 400 mg/L DOC

- Reference substance: Diethylene glycol was used as a reference substance.

Test assay	Blank	RS	TS
TS (mg/L)			1,000
TS (mg DOC/L)	0		400
RS (mg/L)		908.3	
RS (mg DOC/L)	0	399.6	
Water (mL)	2,493	1,950	1,743
Medium (mL)	7.5	7.5	7.5
Inoculum (mL)	500	500	500
Inoculum (mg dw/L)	1	1	1
Mercury chloride (mL)	0	0	0
Stock solution TS (mL)	0		750
Stock solution RS (mL)		543	
pH (prior neutralization)	7.8	6.8	6.8
Liquid volume (mL)	3,000	3,000	3,000

RS=reference substance, TS=test substance.

RESULTS

- **Degradation after 28 days:** 0% by DOC after 28 days
- **Results:** Not inherently biodegradable
- **Remarks:** Degradation of reference substance: 100% DOC after 7 days

CONCLUSIONS Tris(2-hydroxyethyl) isocyanurate is not inherently biodegradable.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks:** Guideline study, essential test conditions available

REFERENCES BASF AG, Labor Oekologie; unveroeffentlichte Unter-suchung, (Original registration No. 1901210, Date:02.11.1990)

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks**

Bioaccumulation

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:**

METHOD

- **Method/guideline:** OECD TG 305C "Bioaccumulation, Test for the degree of Bioconcentration in Fish."
- **GLP:** No
- **Year:** 1978
- **Species:** Carp (*Cyprinus carpio*)
- **Exposure period:** 42 days at 25°C
- **Statistical methods:**
- **Remarks field for Test Conditions:**
  - **Test fish:** *Cyprinus carpio* were acclimated for 14 days at 25°C (average body weight: 23 g, average total length: 10 cm).
  - **Test condition:**
    - **Details of test:** Flow-through method at flow-rate of 400 mL/min during test period
    - **Test concentration:** Two exposure concentrations were set at 2.5 and 0.25 mg/L taking account of the acute toxicity value to *Oryzias latipes* (48h-LC_{50}; >1,000 mg/L) in the preliminary test and the detection limit of analytical method used.
    - **Dispersant:** Not used
    - **Stock and test solutions:** The stock solution was prepared by dissolving 10 g of test substance in 1L water (10,000 mg/L). The stock solution was diluted with water for the preparation of test solution.
    - **Exposure vessel type:** One-hundred L aquaria
    - **Water chemistry during the test:**

      DO: 5.8-7.1 mg/L at 2.5 mg/L
      6.2-7.1 mg/L at 0.25 mg/L
    - **Test temperature range:** 25 +/- 2 ℃
  - **Analytical method:** Gas chromatograph was used for analysis. The concentrations of test substance were determined twice a week and three test fishes were picked up every 2 weeks, two of which were subjected to analysis of concentration in test fish. Bioconcentration factor was calculated as ratio of the concentration of test substance of fish to medium.

RESULTS

- **Remarks field for results:**
  - **Table showing the mean test concentration**

Nominal concentration (mg/L)	Measured concentration (mg/L)			
	2-week	3-week	4-week	6-week
2.5	2.69	2.58	2.57	2.33
0.25	0.237	0.242	0.250	0.232

- **Bioconcentration factor**
  - **Table showing the bioconcentration factor during the experiment**

Nominal concentration (mg/L)		Measured concentration (mg/L)			
		2-week	3-week	4-week	6-week
2.5	1	=<0.16	=<0.16	=<0.16	=<0.16
	2	=<0.16	=<0.16	=<0.16	=<0.16
0.25	1	=<1.6	=<1.6	=<1.6	=<1.6
	2	=<1.6	=<1.6	=<1.6	=<1.6

- **Elimination** Not conducted

CONCLUSIONS Bioconcentration factor of tris(2-hydroxyethyl) isocyanurate is below 0.16 at 2.5 mg/L and below 1.6 at 0.25 mg/L.

DATA QUALITY

- **Reliabilities:** (2) Valid without restrictions
- **Remarks:** Guideline study, essential test conditions available

REFERENCES Ministry of Economy, Trade and Industry (METI), Japan. Unpublished report

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks:**

ECOTOXICITY

ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd., Purity: 99.7 %, Lot No. GE 01

METHOD

- **Method/guideline followed:** OECD TG 203 " Fish, Acute Toxicity Test"
- **Type:** Semi-static
- **GLP:** Yes
- **Year:** 2000
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka); obtained from commercial hatcheries (Sankyo Fisheries Co. Ltd, 1-1 Ichigaya-tamachi, Shinjuku-ku, Tokyo, Japan).
- **Analytical monitoring:** Measured by capillary electrophoresis at the beginning of the test and at the renewal of the test solution (after 24 h).
- **Exposure period:** 96 h
- **Statistical methods:** Not described
- **Remarks field for Test Conditions:**
  - **Test fish:** Acclimated for 12 days before testing; The group, showed less than 5 % mortality for 7 days before testing, was used; fish with 16.4-21.1 mm in body length, 0.074-0.122 g in body weight were selected.
  - **Test conditions:**
    - **Details of test:** Open system
    - **Dilution water source:** Dechlorinated tap water
    - **Dilution water chemistry:** Hardness: 60 mg/L as $CaCO_3$; pH 7.6 (22.0°C)
    - **Stock and test solutions:** The test substance (2 g) was dissolved in pure water to produce the stock solution of 10,000 mg/L and test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
    - **Concentrations dosing rate, flow-through rate, in water medium:** One concentration of 100 mg/L, and control were tested.
    - **Renewal rate of the test solution:** The test solution was renewed every 24h.
    - **Vehicle/solvent and concentrations:** Not used
    - **Stability of the test substance solutions:** Not described
    - **Exposure vessel type:** All glass 5-L aquaria
    - **Number of replicates, fish per replicate:** One vessel for treatment, 10 fish per replicate
    - **Loading:** About 0.2 g/L
    - **Water chemistry in test:** DO 5.7-8.3 mg/L; pH 7.3-7.8
    - **Lighting:** 16h light/8h darkness cycle
    - **Test temperature range:** 23.3-23.7°C (Containers used for testing were placed in a incubator.)

RESULTS

- **Nominal concentrations (as mg/L):** 0 and 100
- **Measured concentrations (as mg/L):** 91.9(Day 0)-92.0(Day 1)
- **Unit [results expressed in what unit]:** % survival after 24, 48, 72, 96 h
- **Element value:** 96h-LC_{50} is above100 mg/L based on nominal concentration
- **Statistical results:** binomial.
- **Remarks field for Results:**
  - **Biological observations:** No abnormal response at the test concentration and control during the exposure.

– Table showing cumulative mortality:

Nominal concentration (mg/L)	Measured concentration (mg/L)	Cumulative mortality (%)			
		24 h	48 h	72 h	96 h
Control	<0.9	0	0	0	0
100	91.9-92.0	0	0	10	10

– Lowest test substance concentration causing 100% mortality:
Not observed

– Mortality of controls: No mortality at the control

– Abnormal responses: No abnormal responses at the test concentration and control during the exposure

– Reference substance results (if used):
LC_{50} of copper sulfatepentahydrate at 96 h: 1.5 mg/L

– **Any observations, such as precipitation that might cause a difference between measured and nominal values:** Not described

CONCLUSION 96h-LC_{50} of tris(2-hydroxyethyl) isocyanurate was greater than 100 mg/L and 96h-LC_{10} of that was 100 mg/L.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Guideline study under GLP

REFERENCES

Ministry of the Environment (MOE), Japan (2000). Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

OTHER

- **Last changed**
- **Order number for sorting**
- **Remarks field for General Remarks**

ACUTE TOXICITY TO AQUATIC INVERTEBRATE

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd, Purity: 99.7 %, Lot No. GE01

METHOD

- **Method/guideline followed:** OECD TG 202, part1 "Daphnia sp., Acute Immobilisation Test"
- **Type:** 48-h immobility, static
- **GLP:** Yes
- **Year:** 2000
- **Species/Strain/Supplier:** *Daphnia magna*; obtained from National Institute for Environmental Studies (NIES), cultured in the laboratory.
- **Analytical monitoring:** Measured by capillary electrophoresis at the beginning and end of the test (48h).
- **Exposure period (h):** 48
- **Statistical methods:** Not described
- **Remarks field for Test Conditions:**
  - **Test organisms:**
    - **Source, supplier, any pre-treatment, breeding method:** Supplied by NIES
    - **Pre-treatment:** The group of parents, which showed less than 5% mortality for 14 days prior to test, was used.
    - **Age at study initiation:** <24h old
  - **Test conditions**
    - **Stock and test solution:** Five hundred mg of test substance was dissolved in 500 mL dilution water to produce the stock solution of 1,000 mg/L and the test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
    - **Renewal rate of the test solution:** Not conducted
    - **Test temperature range:** 20.0-21.0 °C
    - **Exposure vessel type:** 100 mL test solution in a 100 mL glass beaker; 4 beakers per treatment group
    - **Dilution water source:** Elendt M4 medium
    - **Lighting:** <800 lx, 16h light/ 8h darkness cycle
    - **Water chemistry in test:** DO: 7.5-8.6 mg/L, pH: 7.8-8.2
  - **Element (unit) basis:** Immobilisation
  - **Test design:**
    - **Number of replicates:** 4 replicates
    - **Individuals per replicate:** 5
  - **Concentrations:** One concentration of 1,000 mg/L and control were tested.
  - **Method of calculating mean measured concentrations:**
  - **Exposure period:** 48 h
  - **Feeding:** No
  - **Analytical monitoring:** 93 % of the nominal concentration at the beginning and end of the test (48h).

RESULTS

- **Nominal concentrations (as mg/L):** 1,000
- **Measured concentrations (as mg/L):** 930(Day 0)-930(Day 2)
- **Unit (results expressed in what unit):** % immobilisation after 24, 48 h
- **Element value:** 48h- EC_{50} is greater than 1,000 mg/L based on nominal concentration.
- **Statistical results:** Not described
- **Remarks field for Results:**
  - **Biological observations**

Number immobilized as compared to the number exposed:

Nominal concentration (mg/L)	Measured concentration (mg/L)	Cumulative numbers of immobilized *Daphnia* (Percent immobility)	
		24 h	48 h
Control	-	0 (0)	0 (0)
1000	930[a]	0 (0)	0 (0)

a : geometric mean

· **Concentration response with 95 % confidence limits:** Not described
· **Cumulative immobilisation:** 0 % immobility in control and 1,000 mg/L
· **Was control response satisfactory (yes/no/unknown):** Yes
· **Reference substance results:** 48h-EC_{50} of potassium bichromate: 0.57 mg/L

CONCLUSIONS

There was no inhibition of immobilisation and no abnormal response during the exposure, and 48h-EC_{50} was greater than 1,000 mg/L of the concentration used.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Guideline study under GLP

REFERENCES

Ministry of the Environment (MOE), Japan (2000). Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Tokyo Kasei Kogyo Co., Ltd, Purity; 99.7 %, Lot No. GE01

METHOD

- **Method/guideline followed:** OECD TG 201
- **Test type:** Static
- **GLP:** Yes
- **Year:** 2000
- **Species/strain/Supplier:** *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- **Element basis:** Area under the growth curve and growth rate
- **Exposure period:** 72 h
- **Analytical monitoring:** Measured by capillary electrophoresis at beginning and end of the test
- **Statistical methods:** Student t test after confirmation for homogeneity of variances by F test (because a mean value at 1,000 mg/L was compared to that of control).
- **Remarks field for Test Conditions:**
  - **– Test organisms**
    - **· Laboratory culture** Pre-cultured for 4 days under the same conditions as test condition.
  - **– Test Conditions**
    - **· Test temperature range:** 22.3-23.1 °C
    - **· Growth/test medium:** OECD medium
    - **· Shaking:** 100 rpm
    - **· Exposure vessel type:** 100 mL medium in a 300 mL conical flask with a cap which allow ventilation.
    - **· Water chemistry in test (pH) in one replicate of each concentration (at the beginning of the test and after 72h):** pH: 7.9 at beginning of the test and 9.8-9.9 at 72h.
    - **· Stock and test solution:** Five hundred mg of test substance was dissolved in 50 mL pure water to prepare the stock solution of 10,000 mg/L and the test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel.
    - **· Light levels and quality during exposure:** 4,000 lx, continuous
  - **– Test design:**
    - **· Number of replicates:** 3 per treatment
    - **· Concentrations:** One concentration of 1,000 mg/L and control were tested.
    - **· Initial cell number in cells/mL:** 1×10^4

RESULTS

- **Nominal concentrations (as mg/L):** 1,000
- **Measured concentrations (as mg/L):** 954 (Day 0)- 927 (Day 3)
- **Unit [results expressed in what unit]:** Cell density (cells/mL)
- **Element value:** ErC_{50} > 1,000 mg/L (24-72 h); NOEC(r) >= 1,000 mg/L,? EbC_{50} > 1,000 mg/L (0-72 h); NOEC(b) >= 1,000 mg/L calculated based on nominal concentration.
- **Was control response satisfactory:** Yes: mean cell density increased to 2.78×10^6 cells/mL in control after 72 h.
- **Statistical results:** Significant difference was not detected between values at 1,000 mg/L and in control.
- **Remarks field for Results:**
  - **– Biological observations**
    - **· Cell density at each flask at each measuring point:**

Nominal concentration (mg/L)	Measured concentration (mg/L)	Cell concentration for each exposure ($x10^4$ cells/mL)[b]			
		0 h	24 h	48 h	72 h
Control	-	1.0	5.2 ± 0.2	44.6 ± 4.7	278.3 ± 8.5
1,000	927-954[a]	1.0	5.6 ± 0.7	46.0 ± 3.1	270.6±10.5

a : value at start and end of the test
b : mean ± standard deviation

· **Growth curves:**

Percent biomass/growth rate inhibition per concentration:

1.1 % for area under growth curve (0-72 h),
2.0 % for growth rate (24-48 h),
2.5 % growth rate (24-72 h)

· **Reference substance result:** 72h-EbC_{50} of potassium bichromate; 0.423 mg/L

CONCLUSIONS

There was no statistical significant difference in inhibition rate compared with the Control, and 72h-EC_{50} were greater than 1,000 mg/L and 72h-NOEC were more than 1,000 mg/L.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Guideline study under GLP

REFERENCES

Ministry of the Environment (MOE), Japan (2000). Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd, Purity: 99.7 %, Lot No. GE 01

METHOD

- **Method/guideline followed:** OECD TG 211 " *Daphnia magna* Reproduction Test"
- **Test type:** Semi-static
- **GLP:** Yes
- **Year:** 2000
- **Analytical procedures:** Measured by capillary electrophoresis, 1 set (before and after the replacement of the test water) a week.
- **Species/Strain:** *Daphnia magna*; obtained from National Institute for environmental Studies (NIES), cultured in the laboratory.
- **Exposure period:** 21 d
- **Test details:** Water renewal: 3 times a week
- **Statistical methods:** F test and Student t-test
- **Remarks field for Test Conditions:**
  - **Test organisms:**
    - **Source, supplier, any pretreatment, breeding method:** Supplied by NIES
    - **Age at study initiation:** < 24 h old
    - **Pretreatment:** The group of parents, which showed less than 5% mortality for14 days prior to test, was used.
  - **Test conditions**
    - **Stock solutions preparation and stability:** Five hundreds mg of test substance was dissolved in 25 mL pure water to produce 20,000 mg/L stock solution and test solution was prepared by adding the appropriate amount of the stock solution into the dilution water in test vessel. Stability of test solution was confirmed by capillary electrophoresis analysis.
    - **Test temperature range:** 19.8-20.2 °C
    - **Exposure vessel type:** Eighty mL test solution in a 100 mL glass beaker; 10 beakers per treatment
    - **Dilution water source:** Elendt M4 medium
    - **Dilution water chemistry:** Hardness: 220-245 mg/L as $CaCO_3$
    - **Lighting:** < 800 lx, 16 h light/ 8h darkness cycle
    - **Water chemistry in test:** DO: 8.2-8.9 mg/L; pH: 7.2-8.4
    - **Feeding:** *Chlorella vulgaris*, 0.15 mgC/day/individual
  - **Element (unit) basis:** Mean cumulative numbers of juveniles produced per adult (reproduction)
  - **Test design:**
    - **Number of replicates:** 10
    - **Individuals per replicate:** 1
  - **Concentrations:** 100 mg/L.
  - **Method of calculating mean measured concentrations:** Time-weighted mean
  - **Analytical monitoring:** 92-96 % of the nominal concentration at preparation; 93-97 % just before the renewal of the test water.

RESULTS

- **Nominal concentrations (as mg/L):** 100
- **Measured concentrations (as mg/L):** 92-97

– Table on measured concentrations:

Nominal concentration (mg/L)	Measured concentration (mg/L)						
	0 day[a]	2 days[b]	8 days[a]	10 days[b]	20 days[a]	21 days[b]	Mean[c]
Control	<1	<1	<1	<1	<1	<1	-
100	93	93	92	97	96	96	94

a : freshly prepared test solution
b : old test solution before renewal
c : time-weighted mean

- **Unit [results expressed in what unit]:** Mean cumulative numbers of juveniles produced per live adult after 21 d
- **EC_{50}, LC_{50}:** EC_{50} (14d, reproduction) >100 mg/L, EC_{50} (21d, reproduction) >100 mg/L, LC_{50} for parental *Daphnia* (14d) >100 mg/L, LC_{50} for parental *Daphnia* (21d) >100 mg/L calculated based on measured concentrations
- **Statistical results:** Differences in mean cumulative numbers of juveniles produced per adult alive between control and *Daphnia* treated with 100 mg/L were not statistically significant.
- **Remarks field for Results:**
  - **– Cumulative numbers of dead parental Daphnia:** 0 % mortality at control and 100 mg/L
  - **– Time of the first brood production of juveniles:** 7 d at control and 100 mg/L
  - **– Mean cumulative numbers of juveniles produced per live adult:**

Nominal concentration (mg/L)	Measured concentration (mg/L)	Mean cumulative numbers of juveniles produced per live adult	
		14 days	21days
Control	-	59	118
100	92-97[a]	65	118

a : value during the test

– Was control response satisfactory: Yes

CONCLUSIONS There was no statistically significant difference in mean cumulative numbers of juveniles produced per live adult between the treatment group and the control. Hence, 21d-EC_{50} was greater than 100 mg/L and 21d-NOEC was more than 100 mg/L on chronic *Daphnia* reproduction test.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Guideline study under GLP

REFERENCES Ministry of the Environment (MOE), Japan (2000). Unpublished report conducted by Mitsubishi Chemical Safety Institute Ltd.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

HEALTH ELEMENTS

ACUTE ORAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Lot No.00915-1, Purity: 99.0 %

METHOD

- **Method/guideline:** OECD TG 401
- **Test type:** Acute oral toxicity
- **GLP:** Yes
- **Year:** 2001
- **Species:** Rat
- **Strain:** Sprague-Dawley
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0, 500, 1,000, 2,000 mg/kg bw
- **Sex:** Male and female
- **Vehicle:** Water for injection
- **Control group and treatment:** Concurrent vehicle
- **Post exposure observation period:** 14 days
- **Statistical methods:** Not applicable, because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**

· ***Age at study initiation*:** 5 weeks old

· ***No. of animals per sex per dose*:** 5 per sex per dose group

– **Study Design:**

·***Satellite groups and reasons they were added*:** None

· ***Clinical observations performed and frequency*:** Clinical signs were observed just before administration, 30 minutes, 2, 4 and 6 h after administration on the day of treatment. Then each rat was observed once a day from day 2 to day 15. Body weight change was examined on the day of treatment and 1, 3, 7, 10, 14 days after treatment.

RESULTS

- **LD_{50}:** Male: > 2,000 mg/kg bw
  Female: > 2,000 mg/kg bw

REMARKS FIELD FOR RESULTS There was no treatment-related adverse effect.

– ***Body weight:*** No compound-related effect was observed. Body weight changes in treated groups were similar to that of the control.

–***Food/water consumption:*** Not examined

–***Clinical signs:*** No treatment related clinical sign, no death observed.

–***Hematology:*** Not examined

–***Biochemistry:*** Not examined

–***Ophthalmologic findings:*** Not examined

–***Mortality and time to death:*** None

– ***Gross pathology incidence and severity:*** No treatment-related abnormalities.

–***Organ weight changes:*** Not examined

–***Histopathology:*** Not examined

CONCLUSIONS There were no treatment related abnormalities. LD_{50} is greater than 2,000 mg/kg for both sexes.

DATA QUALITY

- **Reliabilities:** (1)Valid without restrictions
- **Remarks field for Data Reliability:** Well conducted guideline study under GLP, carried out by Nihon Bioresearch Inc.

REFERENCES

Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

ACUTE ORAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Purity: ca.99.0 %

METHOD

- **Method/guideline:** Other
- **Test type:** Acute oral toxicity
- **GLP:** No
- **Year:** 1976
- **Species:** Rat
- **Strain:** Sprague-Dawley/Gassner
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** One limit dose; 10,000 mg/kg bw
- **Sex:** Male and female
- **Vehicle:** H_2O
- **Control group and treatment:** None
- **Post exposure observation period:** 14 days
- **Statistical methods:** Not applicable, because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**

· ***Body weight at study initiation:*** Body weight at beginning of the test; male: 250 g
female: 160 g

· ***No. of animals per sex per dose:*** 5 per sex per dose group

– **Study Design:**

· ***Volume administered or concentration:*** 20 mL/kg bw, 50% aqueous solution of test substance

· ***Satellite groups and reasons they were added:*** None

· ***Clinical observations performed and frequency:*** 5 times at day of application, afterwards daily besides weekends until necropsy. Body weight change was examined on the day of treatment and 3, 8, 14 days after treatment.

– **Remarks:** In a dose finding test doses of 316, 1,000 and 3,160 mg/kg bw with 2 animals per dose were used in order to establish the dose for the main study; in this range finding test no mortality occurred. Therefore 10,000 mg/kg bw for the main study was chosen.

RESULTS

- **LD_{50}:** > 10,000 mg/kg bw

REMARKS FIELD FOR RESULTS There was no treatment-related adverse effect.

–***Body weight:*** No compound-related effect was observed.
–***Food/water consumption:*** Not examined
–***Clinical signs:*** Diarrhea was observed.
–***Ophthalmologic findings:*** Not examined
–***Mortality and time to death:*** No mortality was observed.
–***Gross pathology incidence and severity:*** No treatment -related abnormalities
–***Organ weight changes:*** Not examined
–***Histopathology:*** Not examined

CONCLUSIONS *There were no treatment related abnormalities. LD_{50} is greater than 10,000 mg/kg bw for both sexes.*

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Scientifically valid study, but not according to nowadays standard nor to GLP

REFERENCES

BASF Report XXV/444, (01.06.76) and original Lab. Raw Data.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

ACUTE INHALATION TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Purity: 99.0 %

METHOD

- **Method/guideline:** Smyth-Carpentaer, Am. Ind. Hyg. Anal. (1962) 27, 95 on which OECD TG 403, Annex 5 is based.
- **Test type:** Acute dust inhalation toxicity
- **GLP:** No
- **Year:** 1975
- **Species:** Rat
- **Strain:** Sprague-Dawley
- **Route of administration:** Inhalation
- **Doses/concentration levels:** 200 L air/h; 9.32 and 15 mg/L as nominal dust concentration
- **Exposure duration** 8 h
- **Sex:** Male and female
- **Vehicle:** Air; unchanged test substance
- **Control group and treatment:** None
- **Post exposure observation period:** 7 days
- **Statistical methods:** Not applicable, because of no fatality

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**

· ***Age at study initiation*:** Not stated

· ***No. of animals per sex per dose*:** 3 per sex per dose group

– **Study Design:**

·***Volume administered or concentration:*** 200 L air/h; 9.32 and 15 mg/L as nominal dust concentration

·***Satellite groups and reasons they were added*:** None

·***Clinical observations performed and frequency*:**

5 times at day of application, afterwards daily besides weekends until necropsy. Body weight change was examined on the day of treatment and 7 days after treatment.

RESULTS

- **LC_{50}:** > 15 mg/L

REMARKS FIELD FOR RESULTS There was no treatment-related adverse effect.

–***Body weight:*** No compound-related effect was observed.

–***Food/water consumption:*** Not examined

–***Clinical signs:*** No treatment related clinical sign, no death observed.

–***Hematology:*** Not examined

–***Biochemistry:*** Not examined

–***Ophthalmologic findings:*** Not examined

–***Mortality and time to death:*** None

–***Gross pathology incidence and severity:*** No treatment-related abnormalities

–***Organ weight changes:*** Not examined

–***Histopathology:*** Not examined

CONCLUSIONS *No inhalation hazard from volatile parts/dust formation under this testcondition.*

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Scientifically valid study, but not according to nowadays standard nor to GLP.

REFERENCES

BASF Report XXV/444, (01.06.76) and original Lab. Raw Data.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

ACUTE TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Purity: ca. 99.0 %

METHOD

- **Method/guideline:** Other
- **Test type:** Acute intraperitoneal injection
- **GLP:** No
- **Year:** 1976 (conducted)
- **Species:** Mouse
- **Strain:** Ivanovas
- **Route of administration:** Intraperitoneal; injection
- **Doses/concentration levels:** At limit dose (10,000 mg/kgbw)
- **Sex:** Male and female
- **Vehicle:** H_2O
- **Control group and treatment:** None
- **Post exposure observation period:** 14 days

REMARKS FIELD FOR TEST CONDITIONS

– **Test Subjects:**
  · ***Body weigh at study initiation*:** Weight at beginning of the test: 28 g (m); 24 g (f)
  · ***No. of animals per sex per dose*:** 5 of each sex
– **Study Design:**
  · ***Volume administered or concentration*:** 20 mL/kg, 50% aqueous solution of test substance
  · ***Clinical observations performed and frequency*:** 7 times at day of application, afterwards daily besides weekends until necropsy. Body weight change was examined on the day of treatment and 3, 8, 14 days after treatment.
- **Remarks:** In a dose finding test doses of 316; 3,160 and 10,000 mg/kg bw with 2 animals per dose were used in order to establish the dose for the main study; in this range finding test no mortality occurred. Therefore, 10,000 mg/kg bw for the main study was chosen.

RESULTS

- **LD_{50}:** Male: > 10,000 mg/kg bw
  Female: > 10,000 mg/kg bw

REMARKS FIELD FOR RESULTS

–***Body weight:*** No compound-related effect was observed.
–***Food/water consumption:*** Not examined
–***Clinical signs:*** No treatment related clinical sign, no death observed.
–***Hematology:*** Not examined
–***Biochemistry:*** Not examined
–***Ophthalmologic findings:*** Not examined
–***Mortality and time to death:*** None
–***Gross pathology incidence and severity:*** No treatment-related abnormalities.
–***Organ weight changes:*** Not examined
–***Histopathology:*** Not examined

CONCLUSIONS *There were no treatment related abnormalities. LD_{50} is greater than 10,000 mg/kg for both sexes.*

DATA QUALITY

- **Reliabilities:** (2)Valid with restrictions
- **Remarks field for Data Reliability:** Scientifically valid study, but not according to nowadays standard nor to GLP.

REFERENCES BASF Report XXV/444, (01.06.76) and original Lab. Raw Data.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

SKIN IRRITATION/CORROSION

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **pH** Neutral
- **Remarks:** Purity: ca. 99 %

METHOD

- **Method/guideline:** Other
- **Test type:** *in vivo*
- **GLP:** No
- **Year:** 1976
- **Species/Strain:** Rabbit/Gaukler
- **Sex:** Male and female
- **Number of animals per sex per dose:** 2

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**
  - ***Concentration:*** 80% aqueous solution of test substance
  - ***Total dose:*** 0.5 mL/animal
  - ***Vehicle:*** H_2O
  - ***Exposure time period:*** 1, 5, 15 minutes and 20 hours
  - ***Grading scale:*** No effect, Questionable, Slight, Strong, Very strong
  - ***Method remarks:*** Grading for erythema, edema and necrosis

RESULTS

Exposure period	Reading after 24 hours	Reading after 8 days
1 minute	Animal1; questionable erythema	No findings
	Animal2; no findings	
5 minutes	Animal1; questionable erythema Animal2; no findings	No findings
15 minutes	Animal1; questionable erythema	No findings
	Animal2; no findings	
20 hours	Animals 1+2; questionable erythema, localized	No findings

REMARKS FIELD FOR RESULTS .

CONCLUSIONS Tris(2-hydroxyethyl) isocyanurate is not irritating to skin.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Scientifically valid study, but not according to nowadays standard nor to GLP

REFERENCES : BASF Report XXV/444 (01.06.76) and original Lab. Raw data

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

EYE IRRITATION/CORROSION

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **pH** Neutral
- **Remarks:** Purity: ca. 99%

METHOD

Method/guideline: Other

- **Test type:** *in vivo*
- **GLP:** No
- **Year:** 1976
- **Species/Strain:** Rabbit/Gaukler
- **Sex:** Male and female
- **Number of animals per sex per dose** 2

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**
  - ***Dose used:*** 50 mg/animal (as unchanged substance)
  - ***Observation period:*** 1, 24 hours and 8 days
  - ***Control and treatment:*** Talcum powder was used as negative control at the other eye of the animals.
- **Scoring Criteria:**
  - ***Scoring method used:*** No effect, Questionable, Slight, Strong, Very strong
  - ***Tool used to assess score:*** Fluorescein

RESULTS

- **Irritation score:**
  - **Cornea/Iris:** No findings
  - **Conjunctivae:** After 1 hour, slight redness, secretion
  - **Redness/Chemosis:** After 24 hours, no findings

REMARKS FIELD FOR RESULTS. At the end of the observation period (8d) both talcum and THEIC resulted in slight redness in one animal. The other animal showed no reactions.

CONCLUSIONS Tris(2-hydroxyethyl) isocyanurate is not irritating to eyes.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Scientifically valid study but not according to nowadays standard nor to GLP

REFERENCES: BASF Report XXV/444 (01.06.76) and original Lab. Raw data

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

REPEATED DOSE TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Lot No. 00915-1, Purity: 99.0 %

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP:** Yes
- **Year:** 2001
- **Species:** Rat
- **Strain:** Sprague-Dawley
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0, 30, 100, 300, 1,000 mg/kgbw/day
- **Sex:** Male and Female
- **Exposure period:** Males: 49 days (14 days before mating and 35 days including 14 days for mating); Females: 40-46 days (from 14 days prior to mating to day 3 of lactation)
- **Frequency of treatment:** Daily
- **Control group and treatment:** Concurrent vehicle (water for injection)
- **Post exposure observation period** 1 day
- **Statistical methods:** Dunnett's test for numerical data and Chi square test for copulation index and fertility index were used.

REMARKS FIELD FOR TEST CONDITIONS

– ***General remarks:*** This study was conducted to examine both repeated dose toxicity and reproductive/developmental toxicity as an OECD screening combined study. Therefore, hematological and blood chemical examinations, and urinalysis for females were not performed.

– **Test Subjects:**

·***Age at study initiation:*** 10 weeks old

·***No. of animals per sex per dose:*** 12 animals per sex per dose group

– **Study Design:**

· ***Satellite groups and reasons they were added*:** None

· ***Clinical observations performed and frequency*:**

· **Clinical signs:** Twice a day (just before and after administration)

· **Body weight:** Male: Twice a week
Female: Twice a week for pre-mating and mating period, 0, 7, 14, 21st day of pregnancy and 0, 4th day of lactation period.

· **Food consumption:** Male: Twice a week for pre-mating period and after a mating period end.
Female: Twice a week for pre-mating period, 2, 9, 16, 21st day of pregnancy and 4th day of lactation period.

· ***Hematological examinations (only for males):***
Red blood cell count, white blood cell count, platelet count, hemoglobin concentration, hematocrit value, differential leukocyte counts, protrombin time, activated partial thromboplastin time, fibrinogen, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte count.

· ***Blood chemical examinations (only for males):***
Total protein, albumin, A/G ratio, blood urea nitrogen, creatinine, glucose, total cholesterol, total bilirubin, triglyceride, sodium, potassium, chloride, calcium, inorganic phosphorus, alkaline phosphatase, AST, ALT, gamma-GTP.

· ***Urinary examinations (only for males):***
Urinalysis was conducted just before the termination of administration, and following items were examined.
Volume, specific gravity, color, pH, protein, glucose, ketone body,

bilirubin, occult blood, urobilinogen, urinary sediments.

· ***Organs examined at necropsy:***

Males were killed on the day after the administration period. Females were sacrificed on the day 4 of lactation. Females with no delivery were killed 4 days after the delivery expected date. Females with no copulation were sacrificed at the end of mating period.

· **Macroscopic:** All rats were received a full macroscopic examination with tissue collection.

· **Organ weights:** The following organs were weighed at necropsy.
Brain, pituitary, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries were recorded.

· **Microscopic:** The following organs were microscopically observed for control and 1,000 mg/kg bw/day group. Liver and spleen (male only) were also examined for 30, 100 and 300 mg/kg bw/day groups.
Brain, pituitary gland, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries, lung, trachea, pancreas, salivary glands, esophagus, stomach, duodenum, jejunum, ileum, cecum, rectum, colon, lymph node, bladder, uterus, vagina, parathyroids, spinal cord, sciatic nerve, eyes, Harderian glands, mammary gland, bone marrow, seminal vesicle, prostate.

RESULTS

Male	NOAEL =	1,000 mg/kg bw/day
Female	NOAEL =	1,000 mg/kg bw/day

REMARKS FIELD FOR RESULTS

–***Body weight:*** No treatment-related abnormality was observed.

–***Food consumption:*** No treatment-related abnormality was observed.

–***Clinical signs:*** No treatment-related abnormality was observed.

–***Hematology:*** No treatment-related abnormality was observed.

–***Blood chemical analysis:*** No treatment-related abnormality was observed.

–***Urinalysis:*** No treatment-related abnormality was observed.

–***Ophthalmologic findings:*** Not examined

–***Mortality and time to death:*** None

–***Gross pathology incidence and severity:***
No treatment-related abnormality was observed.

–***Organ weight changes:*** No statistically significant differences from controls in any organ was observed.

–***Histopathology:***

Males: No treatment-related abnormality was observed.

Females: Extramedullary hematopoiesis in the liver was noted in two female animals of 1,000 mg/kg bw/day group by histopathological examination.

CONCLUSIONS

Very slight (marginally positive) extramedullary hematopoiesis in the liver was noted histopathologically in two female of 12 animals administered 1,000 mg/kg bw/day. Although the author showed this change was the substance-related one in the original paper, it was considered to be no adverse effect because the change was not statistically significant from control and no other changes were observed at this dose level. No treatment related adverse effect was found up to 1,000 mg/kg bw/day for males. Thus, the NOAEL values for repeated dose toxicity in male and female rats are estimated to be 1,000 mg/kg bw/day.

DATA QUALITY

- **Reliabilities:** (1)Valid without restrictions.
- **Remarks field for Data Reliability:** Well conducted guideline study under GLP, carried out by Nihon Bioresearch Inc.

REFERENCES

Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

TOXICITY TO REPRODUCTION/DEVELOPMENT

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Lot No. 00915-1, Purity: 99.0 %

METHOD

- **Method/guideline:** OECD TG 422
- **Test type:** OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
- **GLP (Y/N):** Yes
- **Year (study performed):** 2001
- **Species:** Rat
- **Strain:** Sprague-Dawley
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0, 30, 100, 300, 1,000 mg/kgbw/day
- **Vehicle:** Water for injection
- **Sex:** Male and Female
- **Exposure period:** Males: 49 days (14 days before mating and 35 days including 14 days for mating); Females: 40-46 days (from 14 days prior to mating to day 3 of lactation.)
- **Frequency of treatment:** Daily
- **Control group and treatment:** Concurrent vehicle (water for injection)
- **Duration of test:** Males: 50 days; Females: from 14 days prior to mating to day 4 of lactation.
- **Statistical methods:** Dunnett's test for numerical data was used.

REMARKS FIELDS FOR TEST CONDITIONS Age at study initiation was 10 weeks old for both sexes. Males were killed on the day after the administration period. Females were sacrificed on the day 4 of lactation. Females with no delivery were killed 4 days after the delivery expected date. Females with no copulation were sacrificed at the end of mating period.

- **Weight at study initiation:** 335-364 g for males, 233-263 g for females
- **Number of animals per dose:** 12 per sex per dose
- **Mating procedures:** Male/female per cage; 1/1, length of cohabitation; at the most 14 days, until proof of pregnancy formation of vaginal plug or sperm in vagina was confirmed.
- **Clinical observations performed and frequency:**
  Parents: twice a day
  Pups: twice a day after birth
- **Parameters assessed during study:**
  Body wt. (Male: Twice a week, Female: Twice a week for pre-mating and mating period, 0, 7, 14, 21st day of pregnancy and 0, 4th day of lactation period.), food consumption (Male: Twice a week for pre-mating period and after a mating period end. Female: Twice a week for pre-mating period, 2, 9, 16, 21st day of pregnancy and 4th day of lactation period.), No. of pairs with successful copulation, copulation index (No. of pairs with successful copulation/No. of pairs mated x 100), pairing days until copulation, frequency of vaginal estrus, No. of pregnant females, fertility index = (No. of pregnant animals/No. of pairs with successful copulation x 100), No. of corpora lutea, No. of implantation sites, implantation index (No. of implantation sites/No. of corpora lutea x 100), No. of living pregnant females, No. of pregnant females with parturition, gestation length, No. of pregnant females with live pups on day 0, gestation index (No. of females with live pups/No. of living pregnant females x 100), No. of pregnant females with live pups on day 4, delivery index (No. of pups born/No. of implantation sites x 100), No. of pups alive on day 0 of lactation,

live birth index (No. of live pups on day 0/No. of pups born x 100), sex ratio (Total No. of male pups/Total No. of female pups), No. of pups alive on day 4 of lactation, viability index (No. of live pups on day 4/No. of live pups on day 0 x 100), body wt. of live pups (on day 0 and 4).

– **Organs examined at necropsy:**

Parent:

Macroscopic: All rats were received a full macroscopic examination with tissue collection.

Organ weights: The following organs were weighed at necropsy. Brain, pituitary, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries were recorded.

Microscopic: The following organs were microscopically observed for control and 1,000 mg/kg group. Liver and spleen (male only) were also examined for 30, 100 and 300 mg/kg bw/day groups.
Brain, pituitary gland, thyroids, heart, thymus, liver, spleen, adrenals, kidneys, testes, epididymides, ovaries, lung, trachea, pancreas, salivary glands, esophagus, stomach, duodenum, jejunum, ileum, cecum, rectum, colon, lymph node, bladder, uterus, vagina, parathyroids, spinal cord, sciatic nerve, eyes, Harderian glands, mammary gland, bone marrow, seminal vesicle, prostate.

Pups: Full macroscopic examinations on all of pups

RESULTS

- **NOAEL (NOEL) and LOAEL (LOEL) maternal toxicity:**
  NOAEL: 1,000 mg/kg bw/day
- **NOAEL (NOEL) and LOAEL (LOEL) foetal toxicity:**
  NOAEL: 1,000 mg/kg bw/day
- **Actual dose received by dose level by sex, if available:**
  0, 100, 300, 1,000 mg/kg bw/day for both sexes
- **Maternal data with dose level (with NOAEL value):**
  No abnormalities were found in all reproductive parameters (fertility index, number of implantations and implantation index) in each dose group.
- **Foetal data with dose level (with NOAEL value):**
  No abnormalities were found in all indexes (No. of pups born, No. of pups alive, pups weight, sex ratio, viability etc.) obtained from pups in each dose group.
- **Statistical results, as appropriate:** All of the above changes were not statistically significant.
- **Remarks for Results.**
  - **Mortality and day of death:** No deaths occurred in all dams through the study period.
  - **Body weight:** No treatment-related abnormality was observed.
  - **Food/water consumption:** No treatment-related abnormality was observed.
  - **Reproductive data:** No treatment-related abnormality was observed.
  - **Fetal data:** No treatment-related abnormality was observed.
  - **Grossly visible abnormalities, and external abnormalities:**
    Proboscis was observed in a stillbirth pup at 300 mg/kg bw/day.
    No treatment related external abnormality was observed among newborns.

CONCLUSIONS There were no treatment related abnormalities. NOAELs for both maternal and foetal toxicity are 1,000 mg/kg bw/day.

DATA QUALITY

- **Reliabilities:** (1)Valid without restrictions.
- **Remarks field for Data Reliability:** Well conducted guideline study under GLP, carried out by Nihon Bioresearch Inc.

REFERENCES

Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Lot No.00915-1, Purity: 99.0 %

METHOD

- **Method/guideline:** OECD TG 471 and Screening Mutagenicity Testing of Chemicals (Japan)
- **Test type:** Bacterial Reverse Mutation assay
- **GLP:** Yes
- **Year:** 2001
- **Species/Strain:** *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 *Escherichia coli* WP2 *uvr*A
- **Metabolic activation:** S9 from rat liver, induced with Phenobarbital and 5,6-benzoflavone
- **Statistical methods:** No statistic analysis

REMARKS FIELD FOR TEST CONDITIONS

– **Study Design:**

· **Concentration:** -S9: 0, 156, 313, 625, 1,250, 2,500, 5,000 ug /plate
+S9: 0, 156, 313, 625, 1,250, 2,500, 5,000 ug /plate

· **Number of replicates:** 2

· **Plates/test:** 3

· **Procedure:** Pre-incubation

· **Solvent:** Water for injection

· **Positive controls:** -S9 mix; 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (TA100, TA98, WP2 uvrA), Sodium azide (TA1535), and 9-Aminoacridine hydrochloride (TA1537)
+S9 mix; 2-Aminoanthracene (all strains)

· **Criteria of evaluating results:** The result was designated "mutagenic" when at least two-fold increase over the control, and dose response-trend or reproducibility were observed.

RESULTS

- **Cytotoxic concentration:** Toxicity was not observed up to 5,000 ug/plate in all strains with or without S9 mix.
- **Genotoxic effects:**

	+	?	-
– With metabolic activation:	**[ ]**	**[ ]**	**[X]**
– Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

REMARKS FIELD FOR RESULTS.

CONCLUSIONS Bacterial reverse mutation tests showed negative results with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Well conducted guideline study under GLP, carried out by Biosafety Research Center, Foods, Drugs and Pesticides (An-pyo Center, Japan).

REFERENCES : Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd., Purity: >82 %

METHOD

- **Method/guideline:** According to the method of Howorth, S. et al.(1983); Environ. Mutagen., 5, suppl. 1, 3-142
- **Test type:** Bacterial Reverse Mutation assay
- **GLP:** No data
- **Year:** 1992
- **Species/Strain:** *Salmonella typhimurium* TA97, TA98, TA100, TA1535, TA1537
- **Metabolic activation:** S9 from Aroclor 1254-induced rat and Syrian hamster liver
- **Statistical methods:** No statistic analysis

REMARKS FIELD FOR TEST CONDITIONS

– **Study Design:**

· **Concentration:** -S9: 0, 100, 333, 1,000, 3,333, 10,000 ug /plate
+S9: 0, 100, 333, 1,000, 3,333, 10,000 ug /plate

· **Number of replicates:** 2

· **Plates/test:** 3

· **Procedure:** Pre-incubation

· **Solvent:** Water

· **Positive controls:** -S9 mix; 4-nitro-o-phenylenediamine (TA98, TA1538), Sodium azide (TA1535, TA100), and 9-Aminoacridine hydrochloride (TA97, TA1537)
+S9 mix; 2-Aminoanthracene (all strains)

· **Criteria of evaluating results:** The result was designated "mutagenic" when at least two-fold increase over the control, and dose response-trend or reproducibility were observed.

RESULTS

- **Cytotoxic concentration:** Toxicity was not observed up to 10,000 ug/plate in all strains with or without S9 mix.
- **Genotoxic effects:**

	+	?	-
– **With metabolic activation:**	**[ ]**	**[ ]**	**[X]**
– **Without metabolic activation:**	**[ ]**	**[ ]**	**[X]**

REMARKS FIELD FOR RESULTS .

CONCLUSIONS Bacterial reverse mutation tests showed negative results with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** (2)Valid with restrictions
- **Remarks field for Data Reliability:** Data reliability was judged valid with restrictions due to low purity of test substance.

REFERENCES : Zeiger, E. et al. (1992) Environ. Mol. Mutagen., 19, Suppl.21, 2-141.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: NISSAN CHEMICAL INDUSTRIES, LTD., Lot No. 00915-1, Purity: 99.0 %

METHOD

- **Method/guideline:** OECD TG 473 and Screening Mutagenicity Testing of Chemicals (Japan)
- **Test type:** *In vitro* Mammalian Chromosomal Aberration Test
- **GLP:** Yes
- **Year:** 2001
- **Species/Strain:** CHL/IU cells
- **Metabolic activation:** S9 from rat liver, induced with Phenobarbital and 5,6-benzoflavone
- **Statistical methods:** No statistic analysis

REMARKS FIELD FOR TEST CONDITIONS

– **Study Design:** For continuous treatment, cells were treated for 24 without S9. For short-term treatment, cells were treated for 6 h with and without S9 and cultivated with fresh media for 18 h.

· **Concentration:** -S9 (24hr continuous treatment): 0, 653, 1,306, 2,612 ug/mL
-S9 (short-term treatment): 0, 653, 1,306, 2,612 ug/mL
+S9 (short-term treatment): 0, 653, 1,306, 2,612 ug/mL

· **Plates/test:** 2

· **Solvent:** Physiological saline

· **Positive controls:** -S9 mix; Mitomycin C
+S9 mix; Cyclophosphamide

· **Criteria of evaluating results:** The results were considered to be negative if the incidence was less than 4.9%, equivocal if it was between 5.0 and 9.9%, and positive if it was more than 10.0%.

RESULTS

- **Cytotoxic concentration:** Not observed
- **Genotoxic effects:**

	clastogenicity			polyploidy		
	+	?	-	+	?	-
– **With metabolic activation:**	[ ]	[ ]	[X]	[ ]	[ ]	[X]
– **Without metabolic activation:**	[ ]	[ ]	[X]	[ ]	[ ]	[X]

REMARKS FIELD FOR RESULTS Structural chromosomal aberrations and polyploidy were not induced up to a maximum concentration tested under conditions of continuous treatment and short-term treatment with and without an exogenous metabolic activation system.

CONCLUSIONS Chromosomal aberration test in CHL/IU cells showed negative results with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** (1) Valid without restrictions
- **Remarks field for Data Reliability:** Well conducted guideline study under GLP, carried out by Biosafety Research Center, Foods, Drugs and Pesticides (An-pyo Center, Japan).

REFERENCES :

Ministry of Health, Labour and Welfare (MHLW), Japan (2001) Toxicity Testing Reports of Environmental Chemicals, 8, 837-865.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd., Purity: >82 %

METHOD

- **Method/guideline:** Other: NTP's mutagenic testing program
- **Test type:** *In vitro* Mammalian Chromosomal Aberration Test
- **GLP:** No data
- **Year:** 1990
- **Species/Strain:** CHO cells
- **Metabolic activation:** S9mix from Aroclor 1254-induced rat liver
- **Statistical methods:** Dunnett's method was used.

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:** Treatment period: 8h(-S9) or 2h(+S9)
  Harvest time: 10.5h(-S9) or 12h(+S9) from the beginning of the treatment
- **Concentration:** -S9 (8h): 0, 402, 1,210, 4,020 ug/mL
  +S9 (2h): 0, 381, 1,140, 2,290, 3,810 ug/mL
- **Dose selection:** Test concentrations for the chromosomal aberration test were empirically chosen based on toxicity and cell cycle delay as noted in the *in vitro* sister chromatid exchange assay. No further details on dose selection were reported.
- **Plates/test:** 2
- **Solvent:** Water
- **Positive controls:** -S9 mix; Mitomycin C
  +S9 mix; Cyclophosphamide
- **Criteria of evaluating results:** The total percent cells with aberrations (simple, complex, other) were analyzed, and the positive response was defined as the case for which the P value, adjusted by Dunnett's method, was <0.05.

RESULTS

- **Cytotoxic concentration:** Not observed
- **Genotoxic effects:**

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

REMARKS FIELD FOR RESULTS Chromosomal aberrations were not induced up to a maximum concentration tested under conditions with and without an exogenous metabolic activation system.

CONCLUSIONS Chromosomal aberration test in CHO cells showed negative results with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Data reliability was judged valid with restrictions due to low purity of test substance.

REFERENCES :

Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-hydroxyethyl) isocyanurate (CAS: 839-90-7)
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd., Purity: >82 %

METHOD

- **Method/guideline:** Other: NTP's mutagenic testing program
- **Test type:** Sister chromatid exchange assay
- **GLP:** No data
- **Year:** 1990
- **Species/Strain:** CHO cells
- **Metabolic activation:** S9mix from Aroclor 1254-induced rat liver
- **Statistical methods:** A linear regression test (trend test) of SCEs per chromosome vs. the log of the dose was used. For individual doses, absolute increases in SCEs per chromosome of 20% or more over the solvent control were considered significant.

REMARKS FIELD FOR TEST CONDITIONS

–Study Design: CHO cells were maintained at 37 °C in McCoy's 5A medium buffered with 20 mM HEPES and supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 50 IU/mL penicillin, and 50ug/ml streptomycin. Tests were carried out with and without *in vitro* metabolic activation system (S9 mix). In tests without metabolic activation, the test substance was left in culture until colcemid addition, whereas with activation the test substance was added along S9 mix for only 2hr at the beginning of the test period.

5-Bromodeoxyuridine (BrdU; 10 uM) was added 2 hr after addition of the test substance (without S9) or immediately after S9 mix plus substance had been removed. The test substance treatment periods were 26hr without S9 and 2 hr with S9.The total incubation time with BrdU was 28-28.5hr, with colcemid (0.1 ug/mL) present during the final 2-2.5hr. Immediately before the cells were harvested, the cell monolayers were examined, and the degree of confluence and availability of mitotic cells were noted. Cells were collected by mitotic shake-off at doses up to the maximum considered likely to yield sufficient metaphase cells for analysis.

Harvesting and preparation of slides were performed according to the air-drying method. The usual Giemsa plus Hoechst 33258 technique was employed for the differential staining of sister chromatids.
50 seconded-division M2 cells were scored for each the top three concentrations of the test substance and for the controls.

- **Concentration:** 0, 386, 1,160, 3,860 ug/mL
- **Dose selection:** The highest dose used was based on solubility or cytotoxicity, with the highest dose scored being that allowing sufficient metaphase cells for analysis at the time of harvest. No further details on dose selection were reported.
- **Solvent:** Water
- **Positive controls:** -S9 mix; Mitomycin C
  +S9 mix; Cyclophosphamide
- **Criteria of evaluating results:** A trend test of the SCEs per chromosome vs. the log of the concentration was used. If at least two doses shoed increases of at least 20% over the control, the result was designated "+".

RESULTS

- **Cytotoxic concentration:** Not observed

- **Genotoxic effects:**

	+	?	-
– With metabolic activation:	**[ ]**	**[ ]**	**[X]**
– Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

REMARKS FIELD FOR RESULTS. Tris(2-hydroxyethyl)isocyanurate did not increase in SCE frequencies at concentrations of 386-3,860 ug/mL with and without an exogenous metabolic activation system.

CONCLUSIONS Sister chromatid exchange assay in CHO cells showed negative results with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** (2) Valid with restrictions
- **Remarks field for Data Reliability:** Data reliability was judged valid with restrictions due to low purity of test substance

REFERENCES: Loveday, K. et al. (1990) Environ. Mol. Mutagen., 16, 272-303.

OTHER

- **Last changed:**
- **Order number for sorting:**
- **Remarks field for General Remarks:**