(c) Species/strain: Mice/B6C3F1
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (in drinking water)
Exposure period: 90 days
Frequency of treatment: Daily
Post exposure observation period:
Dose: 896, 1,792, 5,375 ppm
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment[X];Concurrent vehicle[X];Historical[ ]
NOAEL: 5,375 ppm (male: 1,994 mg/kg/day, female: 2,200mg/kg/day)
LOAEL:
Results: Although increase in water consumption in both sexes and absolute and relative weights of ovaries in females were observed, these changes were considered due to the high sodium content. No adverse effect was observed.
Method: Other
GLP: Yes [X] No [ ] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Remarks: Sodium hippurate was used as a second control in order to have the sodium burden as the top concentration.
Reference: Hazleton U.S.: 1982

(d) Species/strain: Dogs/Beagle
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (in diet)
Exposure period: 6 months
Frequency of treatment: Daily
Post exposure observation period:
Dose: 0 (vehicle), 0.8 % (calculated daily dose: 291 mg/kg)
Control group: Yes [ ]; No [X]; No data [ ];
Concurrent no treatment[ ]; Concurrent vehicle[ ]; Historical[ ]
NOAEL: 0.8 % (291 mg/kg/day)
LOAEL:
Results: There were no changes in body weight gain, organ weight, and sugar and protein in urine. In addition, hematological and histological changes were not observed.
Method: Other
GLP: Yes [ ] No [X] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Reference: Hodge *et al.*: 1965

(e) Species/strain: Dogs/Beagle
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (in diet)
Exposure period: 2 years
Frequency of treatment: Daily
Post exposure observation period:
Dose: 8 % (calculated daily dose: 2,912 mg/kg)
Control group: Yes [ ]; No [X]; No data [ ];

Concurrent no treatment[ ]; Concurrent vehicle[ ]; Historical[ ]

NOAEL:
LOAEL: 8 % (2912 mg/kg/day)
Results: Two of three dogs died after 16 and 21 months on the regimen, respectively. No change or slight increase in body weights was observed. Periodic urinalyses gave normal trace values for sugar and protein. In hematologic study, only a survival dog showed changes, which are low red blood cell counts, hemoglobin values, and hematocrits. There was no change in organ weights (thyroid, liver, brain, lungs, heart, etc.), expect for decrease in kidney weight of two dogs surviving more than 20 months. In these dogs, there was gross evidence of kidney fibrosis. Sections revealed numerous linear streaks of gray fibrous tissue extending from the papillary tip to the cortical surface. Microscopically, similar changes were observed in the kidneys of all three dogs. The collecting tubules were more uniformly and severely involved, but all portions of the nephron were compressed by fibrosis. There were slight focal dilatation and epithelial proliferation in the ducts of Bellini. In survival dog, focal areas of thyroid atrophy were found with lymphocytic infiltration, but without evidence of hyperplasia.
Method: Other
GLP: Yes [ ] No [X] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Reference: Hodge *et al.*: 1965

(f) Species/strain: Rabbits/Albino
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Dermal
Exposure period: Approx. 3 months
Frequency of treatment: 5 days/week
Post exposure observation period:
Dose: 5 ml of 0.8 % or 8 % aqueous suspension
Control group: Yes [ ]; No [X]; No data [ ];
Concurrent no treatment[ ]; Concurrent vehicle[ ]; Historical[ ]
NOAEL: 0.8 %
LOAEL: 8 %
Results: Urinalyses (sugar and protein) and hematological study showed no change. There were no irritation or other adverse effects on the skin. In histological findings of liver and skin from treated and untreated area, no change was observed at the termination of the study. In the kidneys of the rabbits treated with the 8 % isocyanurate suspension, slight dilatation of the ducts of Bellini and mild tubular changes were found.
Method: Other
GLP: Yes [ ] No [X] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Reference: Hodge *et al.*: 1965

(g) Species/strain: Rabbits/Albino
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]

Route of Administration:	Eye application
Exposure period:	Approx. 3 months
Frequency of treatment:	5 days/week
Post exposure observation period:	
Dose:	0.1 ml of 0.8 % or 8 % aqueous suspension
Control group:	Yes [X]; No [ ]; No data [ ]; Concurrent no treatment[X]; Concurrent vehicle[ ];Historical[ ]
NOAEL:	0.8 %
LOAEL:	8 %
Results:	Increase in body weight was observed during the period of the study in all treated groups. No eye injury was caused and no eye irritation was observed in rabbits treated with an 8 % aqueous suspension of the sodium salt.
Method:	Other
GLP:	Yes [ ] No [X] ? [ ]
Test substance:	Sodium isocyanurate, purity: unknown
Reference:	Hodge *et al.*: 1965

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

Type:	Ames test
System of testing:	*Salmonella typhimurium* TA1535, TA1537, TA98, TA100
Concentration:	100 to 1000 µg/plate
Metabolic activation:	With [ ]; Without[ ]; With and Without [X]; No data [ ]
S9:	Hamster liver - Arochlor 1254
Results:	

		+	?	-
Cytotoxicity conc:	With metabolic activation:			
	Without metabolic activation:			
Precipitation conc:				
Genotoxic effects:		+	?	-
With metabolic activation:		[ ]	[ ]	[X]
Without metabolic activation:		[ ]	[ ]	[X]

Method:	Other
GLP:	Yes [ ] No [X] ? [ ]
Test substance:	purity: unknown
Remarks:	
Reference:	Hayworth *et al.*: 1983

Type:	Other: Inductest Pasteur
System of testing:	Induction of bacteriophage Lambda in *Escherichia Coli* K12 en VA UVRB
Concentration:	0.2 to 2000 µg/plate
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	

		+	?	-
Cytotoxicity conc:	With metabolic activation:			
	Without metabolic activation:			
Precipitation conc:				
Genotoxic effects:		+	?	-
With metabolic activation:		[ ]	[ ]	[X]

	Without metabolic activation: [ ] [ ] [X]
Method:	Other
GLP:	Yes [ ] No [X] ? [ ]
Test substance:	purity: unknown
Remarks:	
Reference:	NORSOLOR/APC: 1977

B. NON-BACTERIAL IN VITRO TEST

Type:	Chromosomal aberration test
System of testing:	Chinese hamster lung (CHL/IU) cells
Concentration:	+S9 (short-term treatment): 0, 0.33, 0.65, 1.3 mg/ml -S9 (continuous treatment): 0, 0.33, 0.65, 1.3 mg/ml -S9 (short-term treatment): 0, 0.33, 0.65, 1.3 mg/ml
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
S9:	Rat liver, induced with phenobarbital and 5,6-benzoflavone
Results:	
	Cytotoxicity conc: Not observed Precipitation conc: Genotoxic effects: clastogenicity (+ ? -) polyploidy (+ ? -) With metabolic activation: [ ] [ ] [X] [ ] [ ] [X] Without metabolic activation: [ ] [ ] [X] [ ] [ ] [X]
Method:	Guidelines for Screening Mutagenicity Testing of Chemicals (Japan), and OECD TG (473).
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	purity: 99.5 %
Remarks:	Exposure period: short-term treatment: 6 hr continuous treatment: 24, or 48 hr Positive control: -S9: Mitomycin, +S9: Cyclophosphamide
Reference:	MHW, Japan: 1997

Type:	Mouse lymphoma assay
System of testing:	L 5178 TK +/-
Concentration:	50 to 2000 µg/plate
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	
	Cytotoxicity conc: With metabolic activation: Without metabolic activation: Precipitation conc: Genotoxic effects: + ? - With metabolic activation: [ ] [ ] [X] Without metabolic activation: [ ] [ ] [X]
Method:	Other
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	purity: unknown
Remarks:	
Reference:	Industry ad hoc Committee for Isocyanurates: 1981a

Type:	Sister chromatid exchange assay
System of testing:	CHO cells

Concentration:	93 to 1500 µg/plate
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	
	Cytotoxicity conc: With metabolic activation:
	Without metabolic activation:
	Precipitation conc:
	Genotoxic effects: + ? -
	With metabolic activation: [ ] [ ] [X]
	Without metabolic activation: [ ] [ ] [X]
Method:	Other
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	purity: unknown
Remarks:	
Reference:	Industry ad hoc committee for Isocyanurates: 1981b

* 5.6 GENETIC TOXICITY IN VIVO

Type:	Chromosomal aberration test
Species/strain:	Rats
Sex:	Female [ ]; Male [ ]; Male/Female [ ]; No data [X]
Route of Administration:	Oral (single gavage administration)
Exposure period:	
Doses:	Up to 5000 mg/kg
Results:	
	Effect on mitotic index or P/N ratio:
	Genotoxic effects: + ? -
	[ ] [ ] [X]
Method:	Other
GLP:	Yes [ ] No [X] ? [ ]
Test substance:	Sodium isocyanurate, purity: unknown
Remarks:	Rats were killed 24 and 48 hr after dosing, and bone marrow cells were collected and examined for chromosomal aberrations.
Reference:	Hammond *et al.*: 1985

5.7 CARCINOGENICITY

(a)	Species/strain:	Rats/CD
	Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
	Route of Administration:	Oral (in drinking water)
	Exposure period:	2 years
	Frequency of treatment:	Daily
	Postexposure observation period:	
	Doses:	0 (vehicle), 400, 1,200, 2,400, 5,375 ppm (Estimated daily doses were indicated only for 2,400 and 5,375 ppm (male: 154 and 371 mg/kg/day, female: 266 and 634 mg/kg/day))
	Control group:	Yes [X]; No [ ]; No data [ ]; tap water Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
	Results:	No test article related carcinogenesis.

	Method:	Other
	GLP:	Yes [ ] No [X] ? [ ]
	Test substance:	Sodium isocyanurate, purity: unknown
	Remarks:	Sodium hippurate was administered at the equivalent amount of sodium to the highest dose group as a second control. Treatment-related mortality was observed in some males of highest dose group, which died during the first 12 months of the study. This mortality was due to the development of calculi in the urinary tract. In some males that died on test and in some that were sacrificed at 12 months, there were pathologic changes, including hyperplasia, bleeding, and inflamed ureters, and renal tubular nephrosis. Although slight tubular nephrosis was also observed in a few females of highest dose group during the first 12 months, these animals did not exhibit bladder calculi. Inflammatory lesions in the heart were also apparent in some of the highest dose males that died early.
	Reference:	Cascieri *et al.*: 1985
(b)	Species/strain:	Mice/B6C3F1
	Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
	Route of Administration:	Oral (in drinking water)
	Exposure period:	2 years
	Frequency of treatment:	Daily
	Postexposure observation period:	
	Doses:	0 (vehicle), 100, 400, 1,200, 5,375 ppm
	Control group:	Yes [X]; No [ ]; No data [ ]; Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
	Results:	There was no evidence of test article related carcinogenesis.
	Method:	Other
	GLP:	Yes [X] No [ ] ? [ ]
	Test substance:	Sodium isocyanurate, purity: unknown
	Remarks:	Sodium hippurate was administered at the equivalent amount of sodium to the highest dose group as a second control. Apparent swollen enlarged abdomen was observed at the highest dose groups (both isocyanurate and hippurate). There were no effects on survival, clinical pathology (except for urinary sodium), organ weight, gross and histopathology.
	Reference:	Industry Ad hoc Committee for Isocyanurates, Hazleton laboratories, Report 2169-100 (1986)
(c)	Species/strain:	Rats
	Sex:	Female [ ]; Male [ ]; Male/Female [ ]; No data [X]
	Route of Administration:	Subcutaneous
	Exposure period:	2 years
	Frequency of treatment:	Once a week
	Postexposure observation period:	
	Doses:	Total dose: 6.06 g (approx. daily dose: 8.3 mg/day)
	Control group:	Yes [ ]; No [ ]; No data [X]; Concurrent no treatment[ ]; Concurrent vehicle[ ]; Historical[ ]

	Results:	A lymphosarcoma in lungs has been observed in 1 of the 5 surviving rats after 28 months, and a subdermal lipoma in 1 of the other rats after 30.5 months.
	Method:	Other
	GLP:	Yes [ ] No [X] ? [ ]
	Test substance:	purity: unknown
	Remarks:	
	Reference:	Toxikologische Bewertung.: 1993
(d)	Species/strain:	Mice
	Sex:	Female [ ]; Male [ ]; Male/Female [ ]; No data [X]
	Route of Administration:	Subcutaneous
	Exposure period:	2 years
	Frequency of treatment:	Once a week
	Postexposure observation period:	
	Doses:	Total dose: 0.6 g (estimated daily dose: 0.82 mg/day)
	Control group:	Yes [ ]; No [ ]; No data [X]; Concurrent no treatment[ ];Concurrent vehicle[ ]; Historical [ ]
	Results:	No tumours were observed.
	Method:	Other
	GLP:	Yes [ ] No [X] ? [ ]
	Test substance:	purity: unknown
	Remarks:	
	Reference:	Toxikologische Bewertung.: 1993

*5.8 TOXICITY TO REPRODUCTION

(a)	Type:	Fertility [ ]; One-generation study [ ]; Two-generation study [ ]; Other [X]
	Species/strain:	Rats/Crj: CD (SD)
	Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
	Route of Administration:	Oral (by gavage)
	Exposure period:	Male: 14 days before mating Female: 14 days before mating to day 3 of lactation
	Frequency of treatment:	Daily
	Post exposure observation period:	
	Premating exposure period:	14 days
	Duration of the test:	
	Dose:	0, 10, 40, 150, 600 mg/kg/day
	Control group:	Yes [X]; No [ ]; No data [ ]; Sesame oil Concurrent no treatment[·];Concurrent vehicle[X]; Historical[ ]
	NOEL Parental:	Male: 600 mg/kg/day, Female: 600 mg/kg/day
	NOEL F1 Offspring:	600 mg/kg/day
	NOEL F2 Offspring:	
	Results:	General parental toxicity: Isocyanuric acid indicated no alteration in reproductive parameters including the copulation index, fertility index, gestation length, numbers of corpora lutea or implantations, implantation index, gestation index, delivery index, and behavior at delivery and lactation.

Toxicity to offspring:
There were no significant differences in offspring parameters including number of offspring or live offspring, the sex ratio, live birth and viability indices, and body weight. No external or visceral abnormalities related to the test substance were detected in any of the offspring.

Method: OECD Combined Repeat Dose and Reproductive/ Developmental Toxicity Screening Test
GLP: Yes [X] No [ ] ? [ ]
Test substance: purity: 99.8 %
Remarks:
Reference: MHW, Japan: 1997

(b) Type: Fertility [ ]; One-generation study [ ]; Two-generation study [ ]; Other [X] *Three generation study
Species/strain: Rats/CD
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (in drinking water)
Exposure period: P0: A minimum of 100 days from 36 days of age to mating
F1 and F2: 120 days after weaning
F3: 4 weeks
Frequency of treatment: Daily
Post exposure observation period:
Premating exposure period: A minimum of 100 days
Duration of the test:
Dose: 0 (vehicle), 400, 1,200, 5,375 ppm
Control group: Yes [X]; No [ ]; No data [ ]; tap water
Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
NOAEL Parental: 5,375 ppm (Approx. 370 mg/kg/day for male, 634 mg/kg/day for female)
NOAEL F1 Offspring: 5,375 ppm
NOAEL F2 Offspring: 5,375 ppm
NOAEL F3 Offspring: 5,375 ppm
Results:

General parental toxicity:
No compound related changes were observed in mortality, body weight, food consumption, and gestation length. In pathological and histological findings, there were also no changes.

Toxicity to offspring:
No compound-related changes were observed in mortality, body weights, food consumption litter size, pup survival to weaning, sex ratio, and pup weight. In pathological and histological findings, epithelial hyperplasia with chronic cystitis was observed in a few of high-dose treated males in F2 offsprings, which were attributed to chronic irritation by the calculi in the urinary bladder. In other treated groups, there were no changes.

Method: Other
GLP: Yes [X] No [ ] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown

Remarks: Sodium hippurate was provided an equivalent amount of sodium administered to high-dose sodium isocyanurate animals as second control.
Weanlings from the F1 and F2 litters were randomly selected as parents for the next generation and continued on treatment. Related litters and F3 offsprings were sacrificed 4 weeks after weaning and organ weight measurements and microscopic examination of tissues were carried out.
Reference: Wheeler *et al.*: 1985

(c) Type: Fertility [ ]; One-generation study [ ]; Two-generation study [ ]; Other [X]
Species/strain: Mice/CD-1
Sex: Female [ ]; Male [X]; Male/Female [ ]; No data [ ]
Route of Administration: i.p.
Exposure period: 6 weeks
Frequency of treatment:
Post exposure observation period:
Premating exposure period:
Duration of the test: 6 weeks
Doses: 0 (vehicle), 125 and 250 mg/kg/day
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
NOAEL Parental: 250 mg/kg/day
NOAEL Foetal: 250 mg/kg/day
Results:
General parental toxicity:
Any treatment related effects were not observed in females, mated with sodium isocyanurate treated males.
Toxicity to fetus:
Any toxicity was not observed.
Method: Other
GLP: Yes [ ] No [X] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Remarks: As positive control, methyl methane sulfonate was used at dose of 50 mg/kg/day.
Non-treated females are mated with the treated males every week.
As a result, early resorptions were observed in females mated with males treated with methyl methane sulfonate.
Reference: FMC Corporation: 1972

*5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Species/strain: Rabbits/Dutch belted
Sex: Female [X]; Male [ ]; Male/Female [ ]; No data [ ]
Route of Administration: Oral (by gavage)
Duration of the test: 22 days
Exposure period: Days 6-18 of gestation
Frequency of treatment: Daily
Doses: 0 (vehicle), 50, 200, 500 mg/kg/day

Control group: Yes [X]; No [ ]; No data [ ]; 20 mL/kg water
Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
NOAEL Maternal Toxicity: 50 mg/kg/day
NOAEL teratogenicity: 200 mg/kg/day
Results:
Maternal general toxicity:
Although slight decrease in body weight were observed in mid- and high-dose groups during the treatment period, compensatory weight gains occurred after termination of treatment on day 18. There were no compound related mortality or other adverse reactions.
Pregnancy/litter data:
Foetal data:
The mean number of live fetus/dam and the sex ratio were essentially comparable for all groups. Body weights and crown/rump lengths were reduced slightly in high-dose groups, compared to control. There was no evidence of external or internal malformations or skeletal anomalies.
Method: Other
GLP: Yes [ ] No [X] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Remarks:
Reference: FMC Corporation, unpublished observations

Species/strain: Rats/Sprague-Dawley
Sex: Female [X]; Male [ ]; Male/Female [ ]; No data [ ]
Route of Administration: Oral (by gavage)
Duration of the test: 20 days
Exposure period: Days 6-15 of gestation
Frequency of treatment: Daily
Doses: 0 (vehicle), 200, 1,000, 5,000 mg/kg/day
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment[ ];Concurrent vehicle[X]; Historical[ ]
NOAEL Maternal Toxicity: 5,000 mg/kg/day
NOAEL teratogenicity: 5,000 mg/kg/day
Results:
Maternal general toxicity:
There were no treatment-related effects on maternal appearance, behavior and body weight gain in all groups treated with sodium isocyanurate.
Pregnancy/litter data:
Foetal data:
No teratogenic effects were observed in all groups treated with sodium isocyanurate.
Method: Other
GLP: Yes [X] No [ ] ? [ ]
Test substance: Sodium isocyanurate, purity: unknown
Remarks: Sodium control groups received sodium hippurate at doses of 1,118 and 5,590 mg/kg/day.

In sodium control group, decrease in body weight and crown/rum length, and increase in post-implantation loss and incidence of incomplete ossification were observed.

Reference: Industry ad hoc Committee for Isocyanurates: 1982

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

There is no available data.

B. Toxicodynamics, toxicokinetics

Type: Toxicokinetics

Results: Toxicokinetics study of sodium isocyanurate was performed in rats, using [^{14}C] sodium isocyanurate. The elimination half-life was 30 to 60 min after oral or intravenous administration at 5 mg/kg and 2.5 hr after oral administration at 500 mg/kg. At 5 mg/kg, this chemical was completely absorbed and largely eliminated in urine, while at 500 mg/kg, this chemical was incompletely absorbed and largely eliminated in feces. The remainder of radioactivity in most tissues was below the level of detection (0.1-1.0 μg/g) 7 days after treatment. In second study, rats were administered unlabeled sodium isocyanurate orally at 5 mg/kg/day for 14 days followed by the single exposure on day 15. As results of second study, no bioaccumulation and no significant changes in disposition or metabolism were observed, compared to the single exposure. In excreta, only unchanged isocyanurate was found.

Remarks:

References: Barbee *et al.*: 1983

Type: Toxicokinetics

Results: Toxicokinetics study of sodium isocyanurate was conducted in dogs, using [^{14}C] sodium isocyanurate. Administration was performed at 5 mg/kg by oral or intravenous route and at 500 mg/kg by oral route. At 5 mg/kg, this chemical was completely absorbed and largely eliminated in urine, while at 500 mg/kg, this chemical was only partially absorbed and largely eliminated in feces. Sodium isocyanurate distributed into an apparent volume of distribution of 0.7 L/kg, which is somewhat greater than total body water volume. The elimination half-life was from 1.5 to 2 hr after administration. Dogs were also administered unlabeled sodium isocyanurate orally at 5 mg/kg/day followed by the single exposure of 5 mg/kg radiolabeled sodium isocyanurate on day 15. The remainder of radioactivity in most tissues was below the level of detection (0.1-3.3 μg/g) for all sampling times for both single and repeated dose administration. In excreta, only unchanged isocyanurate was found.

Remarks:

References: Barbee *et al.*: 1984

Type: Toxicokinetics
Results: Toxicokinetics study by dermal route was performed, in which species was not indicated. After dermal application, the ^{14}C-labelled substance is not detectable in the blood and < 0.01% of the administered dose is found in the urine.
Remarks:
References: Toxikologische Bewertung: 1993

* 5.11 EXPERIENCE WITH HUMAN EXPOSURE

Results: Toxicokinetics of isocyanuric acid was investigated in 5 volunteers, who soaked in a swimming pool for 120 minutes. As a result, the cumulative excretion of isocyanuric acid was 0.03-2.8 mg, equivalent to 3.0-3.6 ml of pool water and the elimination half-life is caluculated as 3 hr. On the other hand, recovery of ingested isocyanuric acid is 98 % in urine. No correlation observed between toxicokinetics and gamma glutamyl transpeptidase activity.
Distribution 1 compartment open model.
Remarks:
Reference: Allen *et al.*: 1982

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Appendix 1

scenario 1

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	1,000	9.5.E-08	9.5.E+02	0.1	2.4E+00	9.5.E+00
water	0	4.2.E-02	8.4.E+05	46.5	6.8E+01	8.4.E+02
soil	0	6.0.E-01	9.7.E+05	53.3	7.7E+01	
sediment		3.3.E-02	3.3.E+03	0.2	2.7E-01	6.7.E-02
		total amount	1.8.E+06			

scenario 2

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	0	4.3.E-12	4.3.E+02	0.0	1.1.E-04	4.3.E-04
water	1000	4.6.E-02	9.3.E+05	99.6	7.4.E+01	9.3.E+02
soil	0	2.7.E-05	4.3.E+01	0.0	3.5.E-03	
sediment		3.7.E-02	3.7.E+03	0.4	2.9.E-01	7.3.E-02
		total amount	9.3.E+05			

scenario 3

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	0	7.9.E-10	7.9.E+00	0.0	2.0.E-02	7.9.E-02
water	0	4.2.E-02	8.3.E+05	40.5	6.7.E+01	8.3.E+02
soil	1000	7.6.E-01	1.2.E+06	59.3	9.8.E+01	
sediment		3.3.E-02	3.3.E+03	0.2	2.6.E-01	6.6.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	5.7.E-08	5.7.E+02	0.0	1.5.E+00	5.7.E+00
water	300	4.3.E-02	8.7.E+05	55.1	7.0.E+01	8.7.E+02
soil	100	4.4.E-01	7.0.E+05	44.6	5.6.E+01	
sediment		3.4.E-02	3.4.E+03	0.2	2.7.E-01	6.9.E-02
		total amount	1.6.E+06			

Physico-chemical parameter

molecular weight		129.08	Measured
melting point		330	Measured
vapor pressure [Pa]		5.00E-03	Measured
water solubility [g/m^3]		2700	Measured
log Kow		0.3	Measured
half life [h]	in air	272	Estimated
	in water	8640	Estimated
	in soil	8640	Estimated
	in sediment	8640	Estimated

Temp. []	25

Environmental parameter

		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	1000	1E+10				
bulk water	water	2.0E+10					1000	1000
	particles	1.0E+06			0.04		1500	
	fish	2.0E+05				0.05	1000	
	total	2.0E+10	10	2E+09				
bulk soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8.0E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
bulk sediment	water	8.0E+07					1000	
	solid	2.0E+07			0.06		2400	50000
	total	1.0E+08	0.05	2E+09				

Intermedia Transport 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	0.02	soil water runoff	5E-05
soil water phase diffusion MTC	1E-05	soil solid runoff	1E-08

EXTRACT FROM IRPTC LEGAL FILES

File: 17.01 LEGAL rn : 303375

systematic name:1,3,5-Triazine-2,4,6(1H,3H,5H)-trione
common name :cyanuric acid
reported name :ISOCYANURIC ACID
cas no :108-80-5
area : CAN type : REG

subject	specification	descriptor
USE	OCC	RQR
STORE		
LABEL		

INGREDIENT DISCLOSURE LIST CONCENTRATION 1% WEIGHT/WEIGHT. THE WORKPLACE HAZARDOUS MATERIALS INFORMATION SYSTEM (WHMIS) IS A NATIONAL SYSTEM TO PROVIDE INFORMATION ON HAZARDOUS MATERIALS USED IN THE WORKPLACE. WHMIS IS IMPLEMENTED BY THE HAZARDOUS PRODUCTS ACT AND THE CONTROLLED PRODUCTS REGULATIONS (ADMINISTERED BY THE DEPARTMENT OF CONSUMER AND CORPORATE AFFAIRS). THE REGULATIONS IMPOSE STANDARDS ON EMPLOYERS FORTHE USE, STORAGE AND HANDLING OF CONTROLLED PRODUCTS AND ADDRESS LABELLING AND IDENTIFICATION, EMPLOYEE INSTRUCTION AND TRAINING, AS WELL AS THE UPKEEP OF A MATERIALS SAFETY DATA SHEET (MSDS). THE PRESENCE IN A CONTROLLED PRODUCT OF AN INGREDIENT IN A CONCENTRATION EQUAL TO OR GREATER THAN SPECIFIED IN THE INGREDIENT DISCLOSURE LIST MUST BE DISCLOSED IN THE SAFETY DATA SHEET.
entry date: APR 1991 effective date: 31DEC1987

amendment: CAGAAK, Canada Gazette Part II, 122 , 2 , 551 ,

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File: 17.01 LEGAL rn : 1122611

systematic name:1,3,5-Triazine-2,4,6(1H,3H,5H)-trione
common name :cyanuric acid
reported name :cyanuric acid
cas no :108-80-5
area : RUS type : REG

subject	specification	descriptor
AIR	OCC	MAC CLASS

CLV : 0.5 MG/M3 (AEROSOL) HAZARD CLASS: II
entry date: MAY 1990 effective date: 01JAN1989

amendment: GOSTS*, GOSUDARSTVENNYI STANDART SSSR(STATE STANDARD OF USSR), 12.1.005 , , , 1988

****

File: 17.01 LEGAL rn : 1123035

systematic name:1,3,5-Triazine-2,4,6(1H,3H,5H)-trione
common name :cyanuric acid
reported name :cyanuric acid
cas no :108-80-5
area : RUS type : REG

subject	specification	descriptor
AQ	SURF	MAC CLASS

6.0 MG/L HAZARD CLASS: III
entry date: JUL 1990 effective date: 1JAN1989

amendment: SPNPV*, SANITARNYE PRAVILA I NORMY OKHRANY POVERKHNOSTNYKH VOD OT ZAGRIAZNENIA (HEALTH REGULATION AND STANDARDS OF SURFACE WATER PROTECTION FROM CONTAMINATION), 4630-88 , , , 1988

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File: 17.01 LEGAL rn : 1320069
systematic name:1,3,5-Triazine-2,4,6(1H,3H,5H)-trione
common name :cyanuric acid
reported name :cyanuric acid
cas no :108-80-5
area : USA type : REG

subject	specification	descriptor
CLASS		RQR
MANUF		PRMT

REGISTRATION STANDARD, CHLORINATED ISOCYANURATES, 1987.; Summary - THIS SUBSTANCE IS INCLUDED ON A LIST OF ACTIVE INGREDIENTS FOR WHICH REGISTRATION STANDARDS HAVE BEEN ISSUED AS OF DECEMBER 24, 1988. A REGISTRATION STANDARD IS A DOCUMENT DESCRIBING THE AGENCY'S SCIENTIFIC CONCLUSIONS AND REGULATORY FINDINGS ABOUT CHEMI CALS THAT ARE INGREDIENTS IN PESTICIDE PRODUCTS. REGISTRANTS OF THESE PESTICIDES MUST SUBMIT DATA ON THOSE SUBSTANCES FOR WHICH THEY ARE RESPONSIBLE. INFORMATION WILL BE INCLUDED INTO A DATABASE WHICH WILL ALLOW EPA TO EVALUATE HEALTH AND ENVIRONMENTAL E FFECTS AND DETERMINE APPROPRIATE REREGISTRATION STANDARDS. THIS LIST STATES THE REGISTRATION STANDARD TITLE AND THE YEAR OF THE ISSUANCE OF THE REGISTRATION STANDARD.
entry date: JAN 1992 effective date: 1988

title: FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT: PESTICIDES FOR WHICH REGISTRATION STANDARDS HAVE BEEN ISSUED. LIST A.
original : FEREAC, Federal Register, 54 , 34 , 7740 , 1989
amendment: FEREAC, Federal Register, 54 , 34 , 7740 , 1989

FOREWORD INTRODUCTION

1-Chloro-2-nitrobenzene

CAS: 88-73-3

SIDS Initial Assessment Report

For

SIAM 13

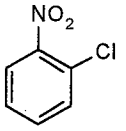
(Bern, Switzerland, 6-9 November 2001)

1. Chemical Name:	1-Chloro-2-nitrobenzene
2. CAS Number:	88-73-3
3. Sponsor Country:	Germany Name of lead organization: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Address: Postfach 12 06 29, D- 53048 Bonn- Bad Godesberg
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	
7. Review Process Prior to the SIAM:	
8. Quality check process:	
9. Date of Submission:	14. September 2001
10. Date of last Update:	Last literature search (up date): 16 August 2001 (Human Health): databases medline, toxline; searchprofile CAS-No. and special search terms 24 July 2001 (Ecotoxicology): databases CA, biosis; searchprofile CAS-No. and special search terms
11. Comments:	OECD/ICCA - The BUA Peer Review Process Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA

guidelines/instructions for the OECD/ICCA peer review process and includes:

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

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	88-73-3
Chemical Name	1-Chloro-2-nitrobenzene
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

After single oral application 1-chloro-2-nitrobenzene is toxic to moderate toxic (LD_{50}, oral: rat, male: 144, 251or 560 mg/kg bw, rat, female: 263 mg/kg bw); the acute inhalative and dermal toxicity is moderate (LC_{50}, rat: 3200 mg/m^3 (= 495 ppm, vapor/aerosol mixture); LD_{50}, dermal, rat: female: 1320 mg/kg bw, male: 655 mg/kg bw; LD_{50}, dermal, rabbit: 400 mg/kg bw (male: 455 mg/kg bw, female: 355 mg/kg bw): Cyanotic appearance was the predominant symptom for all routes of application.

The documentation of the available studies on skin irritation is incomplete in one case and in two other cases the test substance was applied undissolved or respectively diluted. However, the studies gave no evidence of a skin irritating potential. 1-Chloro-2-nitrobenzene caused slight irritation effects to the eyes of rabbits, which were reversible within 24 hours. Due to the limited and poor quality information available regarding skin sensitization, it cannot be concluded whether or not the chemical has a sensitizing activity.

Target organs of repeated dose toxicity in rats and mice are blood, liver, kidney and spleen with methemogobinaemia as the most sensitive parameter. The repeated dose toxicity was examined in rats and in mice for a period of 13 weeks via whole body inhalation. The NOAEL in rats was not achieved, the LOAEL is 1.1 ppm (7 mg/m^3). In mice, increased liver and kidney weights were observed even at 1.1 ppm and respectively 2.3 ppm. The NOAEL for histopathological injury in mice is 4.5 ppm (28.8 mg/m^3). In a subacute feeding study with mice the NOAEL was 50 ppm (males: 16 mg/kg bw/day; females: 24 mg/kg bw/day).

1-Chloro-2-nitrobenzene showed weak mutagenic activity in bacterial test systems but not in mammalian cell test systems *in vitro*. It was not mutagenic in *Drosophila melanogaster*. In mammalian cells *in vitro*, it showed weak clastogenic activity. The substance induced increased rates of Sister Chromatid Exchanges, whereas the biological relevance of this effect is not yet clear. Intraperitoneal injection into mice resulted in DNA damage in the liver and kidney. The inconsistent results of the available genotoxic studies are typical for nitroaromatics. As a whole 1-chloro-2-nitrobenzene is suspected of being genotoxic, at least a weak clastogen.

1-Chloro-2-nitrobenzene induced tumours in different organs of rats and in the liver of mice. Based on the available studies, which have methodological deficiencies, there is a concern for a carcinogenic potential of 1-chloro-2-nitrobenzene. Following inhalative exposure of F344/N rats and B6C3F1 mice for 13 weeks, only in males 1-chloro-2-nitrobenzene affects the reproductive organs. Performance of a specific study on toxicity to reproduction (NTP continuous breeding protocol) reveals that 1-chloro-2-nitrobenzene was without reproductive toxicity in a different mice strain following oral treatment by gavage despite of significant changes in liver and spleen weight and despite of elevated methaemoglobin levels. Thus, the $NOAEL_{fertility}$ in Swiss CD-1 mice after oral application is 160 mg/kg bw/day whereas the dams showed general toxicity effects at this concentration. Because 1-choro-2-nitrobenzene affected the reproductive organs in systemic toxic doses in male rats and in males of one strain of mice

after subchronic inhalation there is a concern for a reproductive toxicity potential, even if an impairment of reproduction after oral administration in males of a second strain of mice could not be detected.

Developmental toxicity was examined by two studies with Sprague-Dawley rats which have methodology deficiencies. In one study, due to high mortality rate at the highest dose level, only two doses could be evaluated. NOAEL $_{\text{maternal toxicity}}$ is 25 mg/kg bw/day, a NOAEL $_{\text{developmental toxicity}}$ could not be conclusively derived since there was an increase in the number of litters exhibiting specific skeletal variations. In the second study only one dose was applied: NOAEL $_{\text{developmental toxicity}}$ is 100 mg/kg bw/day, a NOAEL maternal toxicity could not be derived. Based on the available studies the overall conclusion is, that there is no indication of developmental toxicity, although there are some limitations within the studies.

Environment

1-Chloro-2-nitrobenzene has a melting point of 32 °C, a solubility in water of 441 mg/l at 20 °C, and a vapour pressure of 4.0 Pa at 20°C. The log Kow was measured to 2.24.

According to Mackay fugacity model level I the main target compartments for 1-chloro-2-nitrobenzene are water (65.4 %) followed by air (32.9 %). 1-Chloro-2-nitrobenzene shows no ready biodegradation in aquatic compartments (OECD 301 C: 8.2% after 14d) but under the conditions of industrial waste water treatment plants removal to > 95 % was observed at one production/processing site. However, this elimination cannot be transferred to other sewage treatment plants. Special tests showed adapted cultures to be able to degrade 1-chloro-2-nitrobenzene in a cometabolic pathway. Bioconcentration factors determined for fish were in the range of 7.0 – 22.3 and thus indicate no significant bioaccumulation potential of 1-chloro-2-nitrobenzene. A calculated Koc suggests the substance to have a medium geoaccumulation potential. In the atmosphere the substance is photodegradable indirectly with a calculated half-life of 187 d.

The acute toxicity has been determined for: fish (*Cyprinus carpio*) with a 96 h-LC_{50} of 25.5 mg/l; daphnia (*Daphnia magna*) with a 24 h-$EC_{50}$of 12 mg/l and a 48 h-EC_{50} of 23.9 mg/l, and *Daphnia carinata* with a 48 h-EC_{50} of 21.3 mg/l; algae (*Chlorella pyrenoidosa*) with a 96 h-EbC_{50} of 6.9 mg/l. With another alga species (*Secendesmus subspicatus*) a 48h-ErC50 of 75 mg/l and a 48h-ErC10 of 19 mg/l was found.

Chronic toxicity has been tested for *Daphnia magna* with a 21 dNOEC of 3 mg/l on reproduction (measured concentration) and for fish (*Pimephales promelas*) in an Early Life Stage Test with a 33 d-NOEC of 0.264 mg/l concerning the endpoint normal larvae (measured concentration). A PNECaqua of 0.026 mg/l is derived using an assessment factor of 10.

In a test with terrestrial plants a 14 d-EC50 in the range of 3.2 - 10 mg/kg soil dry weight was determined for Lactuca sativa regarding the endpoint of growth. APNECsoil of 3.2 µg/kg bw was derived from this value using an assessment factor of 1000.

Exposure

About 111,800 t/a 1-chloro-2-nitrobenzene are produced by about 30 producers worldwide. 1-Chloro-2-nitrobenzene is a basic chemical which is processed chemically to other intermediates in different fields of application. There is currently no information that there is consumer use.

NATURE OF FURTHER WORK RECOMMENDED

Human Health: The substance is a candidate for further work. Due to possible hazards (haemotoxicity, reproductive toxicity, genotoxicty, and carcinogenicity) the exposure situation in occupational settings and consumer settings should be clarified and, if then indicated, a risk assessment should be performed.

Environment: The substance is a candidate for further work. Environmental exposure at the sponsor company is adequately controlled. However, as there are no information on environmental releases from other production / processing sites, exposure assessment should be conducted and, if then indicated, a risk assessment may need to be considered. This is justified because the substance is not readily biodegradable and has a PNECaqua of 26 µg/l.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 88-73-3
IUPAC Name: 1-Chloro-2-nitrobenzene
Molecular Formula: $C_6H_4ClNO_2$

1.2 Purity/Impurities/Additives

The purity of the substance is given with > 99 % w/w.

1.3 Physico-Chemical properties

1-Chloro-2-nitrobenzene is a yellowish substance with a melting point of about 32 °C (Bayer AG 1989). With a density of 1.37 g/cm³ at 22 °C . 1-chloro-2-nitrobenzene is heavier than water (Ullmann 1991). The substance is soluble in water with 441 mg/l at 20 °C (Eckert 1962). The vapour pressure has been tested to 4.0 Pa at 20 °C (Bayer AG 2001a). Log K_{ow} is measured with 2.24 (Leo et al. 1971).

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The world wide (excluding East Europe) production of 1-chloro-2-nitrobenzene amounted to 111,800 tons in 1995 (about 27,000 in West Europe, 19,000 t in USA, 9,000 t in Japan, 39,000 t in China, 15,500 t in India, and 2,300 t in South Korea) by approximately 30 producers. There is no information about production in East European countries (Bayer AG 2001).

1-Chloro-2-nitrobenzene is a basic chemical, used industrially for manufacturing of further intermediates by chlorination, nitration, sulfonation, reduction, and substitution. In the following an overview of further processing products and their percentage is given:

- 2-nitroaniline (31 %), an intermediate mainly for pesticides

- dichlorobenzidine (26 %), 2-nitroanisole (23 %), and 2-chloroaniline (8 %), processed mainly to dyestuffs and pigments

- others (12 %), including the manufacturing of nitrochlorobenzenesulphonic acid, dinitrodiphenyldisulphide, and nitrophenetole which are processed mainly to dyestuffs and pigments, of o-fluoronitrobenzene which is processed mainly to pharmaceuticals, and of nitrophenol an intermediate mainly for pesticides.

These data relate to the above cited world wide production demand in 1995 (Bayer AG 2001).

A direct use of 1-chloro-2-nitrobenzene is not known (Bayer AG 2001).

Production of 1-chloro-2-nitrobenzene takes place by mono-nitration of chlorobenzene in a continuously working closed system. Initially a mixture of chloronitrobenzenes is gained. This mixture is separated by distillation- and crystallisation procedures yielding 1-chloro-2-nitrobenzene with a purity above 99 % (Bayer AG 2001).

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Releases into the environment may occur during production and processing.

Readily available information on exposure from production and processing to the chemical in the Sponsor country at Bayer AG is available.

The exhausts from production and processing of 1-chloro-2-nitrobenzene are connected to air washing units and thermal exhaust purification plants. Thus during normal operation no 1-chloro-2-nitrobenzene is emitted. Following the Official German Emission Declaration in year 2000, less than 25 kg/a 1-chloro-2-nitrobenzene were emitted into the atmosphere (Bayer AG 2001).

Waste water leaving the production and processing facilities are pretreated before reaching the industrial waste water treatment plant. 1-Chloro-2-nitrobenzene is monitored daily at the influent and the effluent of the waste water treatment plant.