Cyanotic appearance was the predominant appearance for all three routes of application.

The documentation of the available studies on skin irritation is incomplete in one case and in the two other cases the test substance was applied undissolved or respectively diluted. However, the studies gave no evidence of a skin irritating potential of 1-chloro-2-nitrobenzene.

1-Chloro-2-nitrobenzene caused slight irritational 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.

The repeated dose toxicity was examined in rats and in mice for a period of 13 weeks via whole body **inhalation**. As target organs liver, kidney and spleen were identified in both species, and furthermore, in rats erythrocytes and the nasal cavity respiratory epithelium. The NOAEL in rats was not achieved, the LOAEL is 1.1 ppm (7 mg/m³); In mice, increased liver and kidney weights were observed even at 1.1 ppm and 2.3 ppm, respectively. The NOAEL for histopathological injury in mice is 4.5 ppm (28.8 mg/m³).

In a subacute **feeding** study with mice target organs were blood, spleen and liver. 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 genotoxic tests as described above are typical for nitroaromatics. As a whole 1-chloro-2-nitrobenzene is suspected of being genotoxic, or at least a weak clastogen.

1-Chloro-2-nitrobenzene showed tumours in different organs of rats and in the liver of mice. Overall taking into consideration the results of the genotoxicity tests,and the resulsts of the available lmited studies in rats and mice, 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 methemoglobin 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. $NOAEL_{maternal\ toxicity}$ is 25 mg/kg bw/day, a $NOAEL_{developmental\ toxicity}$ 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: $NOAEL_{developmental\ toxicity}$ 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.

6 RECOMMENDATIONS

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, national or regional exposure information gathering and 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.

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

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I U C L I D Data Set

Existing Chemical	ID: 88-73-3
CAS No.	88-73-3
EINECS Name	1-chloro-2-nitrobenzene
EC No.	201-854-9
TSCA Name	Benzene, 1-chloro-2-nitro-
Molecular Formula	C6H4ClNO2
Producer Related Part	
Company:	Bayer AG
Creation date:	08-JUN-1993
Substance Related Part	
Company:	Bayer AG
Creation date:	08-JUN-1993
Memo:	OECD HPV Chemicals Programme, SIDS Dossier, approved at SIAM 13 (6-9 November 2001)
Printing date:	26-NOV-2003
Revision date:	02-JUN-1994
Date of last Update:	26-NOV-2003
Number of Pages:	96
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

Type: cooperating company
Name: ACNA C.O.
Town: 17010 Cengio (SV)
Country: Italy

Type: cooperating company
Name: Chemie AG Bitterfeld-Wolfen
Town: 06749 Bitterfeld-Wolfen
Country: Germany

Type: cooperating company
Name: Hoechst AG
Town: 65903 Frankfurt/Main
Country: Germany

Type: cooperating company
Name: Monsanto
Town: 1150 Brussels
Country: Belgium

Type: cooperating company
Name: Rhone-Poulenc Chimie
Street: 25 quai Paul Doumer
Town: 92408 Courbevoie Cedex
Country: France

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

1.1.1 General Substance Information

Substance type: organic
Physical status: solid
Purity: > 99 - % w/w

Remark: cooperating companies for the Existing Chemical Regulation:
Hoechst AG, Germany
Chemie AG Bitterfeld-Wolfen, Germany
Monsanto Europe S.A., Belgium
Rhone-Poulenc Chimie, France
ACNA Chimica Organica, Italy
Flag: Critical study for SIDS endpoint
16-NOV-2000

1.1.2 Spectra

1.2 Synonyms and Tradenames

1-CHLORO-2-NITROBENZOL

Flag: Critical study for SIDS endpoint
27-JUL-2001

1-NITRO-2-CHLORBENZOL

Flag: Critical study for SIDS endpoint

2-CHLOR-1-NITROBENZOL

Flag: Critical study for SIDS endpoint

2-CHLORNITROBENZOL

Flag: Critical study for SIDS endpoint

2-NITRO-1-CHLORBENZOL

Flag: Critical study for SIDS endpoint

2-NITROCHLORBENZOL

Flag: Critical study for SIDS endpoint

BENZENE, 1-CHLORO-2-NITRO-

Flag: Critical study for SIDS endpoint

CHLOR-O-NITROBENZOL

Flag: Critical study for SIDS endpoint

O-CHLORNITROBENZOL

Flag: Critical study for SIDS endpoint

O-NITROCHLORBENZOL

Flag: Critical study for SIDS endpoint

OCNB

Flag: Critical study for SIDS endpoint

ONCB

Flag: Critical study for SIDS endpoint

1.3 Impurities

Remark: Dinitrochlorobenzene : max. 0.01 %
p-Nitrochlorobenzene : max. 0.2 %
water : max. 0.1 %

1.4 Additives

1.5 Total Quantity

1.6.1 Labelling

Labelling:	provisionally by manufacturer/importer
Symbols:	(T) toxic (N) dangerous for the environment
R-Phrases:	(24/25) Toxic in contact with skin and if swallowed (40) Possible risks of irreversible effects (43) May cause sensitization by skin contact (51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (62) Possible risk of impaired fertility
S-Phrases:	(28) After contact with skin, wash immediately with plenty of water and soap, if possible with Polyethylenglykol 400, too (36/37) Wear suitable protective clothing and gloves (45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible) (61) Avoid release to the environment. Refer to special instructions/Safety data sets
Remark:	Classification by EEC is required
Flag:	Critical study for SIDS endpoint

18-JUN-2001

1.6.2 Classification

Classified:	provisionally by manufacturer/importer
Class of danger:	carcinogenic, category 3
R-Phrases:	(40) Possible risks of irreversible effects
Flag:	Critical study for SIDS endpoint

28-MAR-2000

Classified:	provisionally by manufacturer/importer
Class of danger:	dangerous for the environment
R-Phrases:	(51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Flag:	Critical study for SIDS endpoint

28-MAR-2000

Classified:	provisionally by manufacturer/importer
Class of danger:	harmful
R-Phrases:	(62) Possible risk of impaired fertility
Remark:	due to classification according to TRGS 905 (DE): risk of impaired fertility, category 3
Flag:	Critical study for SIDS endpoint

25-JUN-2001

Classified:	provisionally by manufacturer/importer
Class of danger:	irritating
R-Phrases:	(43) May cause sensitization by skin contact
Flag:	Critical study for SIDS endpoint

03-APR-2000

Classified:	provisionally by manufacturer/importer
Class of danger:	toxic
R-Phrases:	(24/25) Toxic in contact with skin and if swallowed
Remark:	Classification by EEC is required

Flag: Critical study for SIDS endpoint
28-MAR-2000

1.6.3 Packaging

1.7 Use Pattern

Type: type
Category: Use in closed system

Flag: Critical study for SIDS endpoint

Type: industrial
Category: Chemical industry: used in synthesis

Flag: Critical study for SIDS endpoint

Type: use
Category: Intermediates

Flag: Critical study for SIDS endpoint

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: MAK (DE)

Remark: carcinogenic category 3
risk of cutaneous absorption
risk of impaired fertility, category 3
Source: TRGS 905 (DE)
Flag: Critical study for SIDS endpoint
18-JUN-2001

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 2 (water polluting)

1.8.4 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: yes

Remark: Appendix I, No. 2
16-JUL-2001

1.8.5 Air Pollution

Classified by: other: producer according to TA-Luft (DE)

Number: 3.1.7 (organic substances)
Class of danger: I

1.8.6 Listings e.g. Chemical Inventories

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

1.11 Additional Remarks

1.12 Last Literature Search

Type of Search: Internal and External

Remark: Environmental, ecotoxicology : November 2000
Toxicology: April 1999
25-JUN-2001

1.13 Reviews

Memo: BUA Report No. 2 (o-Chloronitrobenzene), VCH, Weinheim, Oct. 1985

25-JUN-2001

2.1 Melting Point

Value: 32 degree C

Remark: solidifying point
Flag: Critical study for SIDS endpoint
27-JUL-2001 (11)

Value: 31.7 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

Value: >= 31.7 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (37)

Value: 33 degree C

25-JUN-2001 (103)

2.2 Boiling Point

Value: 245.5 degree C at 1000 hPa

Flag: Critical study for SIDS endpoint
25-JUN-2001 (103)

Value: 243 degree C at 1013 hPa

12-JUL-2001 (12)

Value: 245 degree C at 1013 hPa

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

Value: 370 degree C
Decomposition: yes

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

2.3 Density

Type: density
Value: 1.368 g/cm³ at 22 degree C

Flag: Critical study for SIDS endpoint
27-JUL-2001 (103)

Type: density
Value: 1.32 g/cm³ at 70 degree C

Source: Hoechst AG Frankfurt/Main (reference not available)
11-JUL-2001 (37)

Type: density
Value: 1.294 g/cm³ at 90.5 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: = .04 hPa at 20 degree C
Decomposition: no

Method: Directive 84/449/EEC, A.4 "Vapour pressure"
Year: 2001
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: 0.07 hPa at 25 °C
Flag: Critical study for SIDS endpoint
27-JUL-2001 (10)

Value: .0575 hPa at 20 degree C

25-JUN-2001 (16)

Value: 6 hPa at 20 degree C

24-NOV-2000 (25)

Value: 2 hPa at 67.6 degree C

14-SEP-2000 (1)

Value: 49.8 hPa at 150 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

2.5 Partition Coefficient

log Pow: 2.24

Method: other (measured)

Flag: Critical study for SIDS endpoint
30-JUL-2001 (58)

log Pow: 2.46

Method: other (calculated)
Year: 2000

Remark: Calculation KOWWIN v1.66 (2001)
Flag: Critical study for SIDS endpoint
25-JUN-2001 (94)

2.6.1 Solubility in different media

Solubility in: Water
Value: .441 g/l at 20 degree C

Flag: Critical study for SIDS endpoint
27-JUL-2001 (27)

Solubility in: Water
Value: .43 g/l at 20 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
27-JUL-2001 (37)

Solubility in: Water
Value: .59 g/l at 20 degree C

27-JUL-2001 (16)

2.6.2 Surface Tension

2.7 Flash Point

Value: 127 degree C
Type: closed cup

Flag: Critical study for SIDS endpoint
25-JUN-2001 (103)

Value: 124 degree C

27-JUL-2001 (16)

Value: 124 degree C

Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

Value: 128 degree C
Type: closed cup

Method: other: DIN 51758

12-JUL-2001 (12)

2.8 Auto Flammability

Value: 470 degree C

Method: other: DIN 51794

Remark: ignition temp.
Flag: Critical study for SIDS endpoint
12-JUL-2001 (12)

Value: > 450 degree C

Source: Hoechst AG Frankfurt am Main, (Reference not available)
25-JUN-2001 (37)

Value: 487 degree C

Remark: Zuendtemperatur
Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

2.9 Flammability

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Dissociation Constant

2.13 Viscosity

2.14 Additional Remarks

Remark: Untere Explosionsgrenze: 1.15 Vol-%
Obere Explosionsgrenze: 13.1 Vol-%
Gefährliche Zersetzungsprodukte: Nitrose Gase, Chlorwasserstoff
Unverträgliche Substanz: Chlornitrobenzole reagieren mit Reduktionsmitteln.
Source: Hoechst AG Frankfurt/Main, (Reference not available)
25-JUN-2001 (38)

3.1.1 Photodegradation

Type:	other: air, indirect photolysis
Method:	Calculation of the atmospheric oxidation of 1-chloro-2-nitrobenzene by hydroxyl radicals (AOPWIN v1.90, 2001)
Result:	OH rate constant: 0.1714 E-12 cm3/molecule x sec Half-life : 187.2 days (12 h day; 0.5 E6 OH/cm3)
Reliability:	(2) valid with restrictions Accepted calculation method
Flag:	Critical study for SIDS endpoint

12-JUL-2001 (93)

Type:	water
Light source:	other: mercury high pressure lamps
Light spect.:	> 290 nm
DIRECT PHOTOLYSIS	
Degradation:	= 0 % after 180 minute(s)
Method:	other (measured)
Year:	1987
GLP:	no
Test substance:	other TS: 1-chloro-2-nitrobenzene
Method:	irradiation of TS in aqueous solution in the absence and in the presence of TiO2; HPLC analysis
Result:	quantitative degradation of TS was observed only in the presence of TiO2
Reliability:	(3) invalid no detailed description of method, test conditions, and results

12-JUL-2001 (48)

3.1.2 Stability in Water

Remark:	Based on the chemical structure of the compound hydrolysis is not expected under environmental conditions
Flag:	Critical study for SIDS endpoint

25-JUN-2001

3.1.3 Stability in Soil

3.2.1 Monitoring Data (Environment)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

Media:	air - biota - sediment(s) - soil - water
Method:	Calculation according Mackay, Level I
Year:	1991

Remark: Mackay, Calculation of the environmental distribution of 1-chloro-2-nitrobenzene according to fugacity model level I (1991)
Input parameter:
Temperature: 20°C
Vapor pressure: 4.0 Pa
Water solubility: 441 mg/l
log Kow: 2.24
Entry of chemical: 1 mol
Result: Calculated distribution between environmental compartments: water 65.4 %, air 32.9 %, soil 0.9 %, sediment: 0.8 %, susp. sediment: < 0.1 %, fish: < 0.1 %
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
26-NOV-2003

Media: water - air
Method: other (calculation): Henry constant

Result: H = 1.43 Pa m3 mol-1
Flag: Critical study for SIDS endpoint
27-JUL-2001 (61)

Media: water - soil
Method: other (calculation): SCR-PCKOCWIN v1.66
Year: 2000

Result: Koc = 315.5
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
10-AUG-2001 (95)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: other: sludge samples from different sewage plants, rivers, bays and a lake, non adapted
Concentration: 30 mg/l related to Test substance
Degradation: 8.2 % after 14 day(s)

Method: other: Japanese Guideline by MITI of 1974; corresp. OECD 301 C Modified MITI Test I
GLP: no data
Test substance: other TS: no purity given

Remark: Inoculum added: 30 mg/l; BOD measurement
Difference to OECD 301C: Initial test substance concentration 30 mg/l instead of 100 mg/l
Reliability: (1) valid without restriction
Test procedure according to national standards
Flag: Critical study for SIDS endpoint
15-JUL-2002 (64)

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Concentration: 200 mg/l related to DOC (Dissolved Organic Carbon)

Kinetic: 5 day(s) 80 %
10 day(s) > 90 %

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1982
GLP: no

Remark: Elimination by Stripping
Source: Hoechst AG Frankfurt/Main
Reliability: (4) not assignable
Original reference not available
25-JUN-2001 (39)

Type: aerobic
Inoculum: activated sludge
Concentration: 200 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: < 10 % after 15 day(s)
Kinetic: 5 day(s) < 10 %
10 day(s) < 10 %

Method: other: Respirometer Test
Year: 1982
GLP: no

Source: Hoechst AG Frankfurt/Main
Reliability: (4) not assignable
Original reference not available
25-JUN-2001 (39)

Type: aerobic
Inoculum: predominantly domestic sewage, adapted
Degradation: 0 % after 20 day(s)
Result: under test conditions no biodegradation observed

Method: other: comparable to OECD Guide-line 301 D
Year: 1977
GLP: no

Remark: related to BOD
Reliability: (4) not assignable
Original reference not available
12-JUL-2001 (9)

Type: aerobic
Inoculum: other: activated sludge, non-adapted and adapted

Method: other: see remarks
GLP: no
Test substance: other TS: > 99.9 % purity

Method: 3 methods were applied:
1) Revised OECD test, 1971 (Determination of the Biodegradability of Anionic Surface Active Agents)
2) Repetitive Die Away Test: Blok, 1979 (A repetitive Die Away test combining several biodegradability test procedures; Int. Biodeterior. Bull. 15, 57-63)
3) Pitter test (Pitter (1976): Determination of biological degradability of organic substances, Water Res. 10, 231-235.)
Result: t1/2 >> 4 weeks

3.1 Environmental Exposure

3.1.1 General Discussion

Isocyanuric acid is not readily biodegradable (OECD 301C: 0 % after 14d) and stable in water. Direct photodegradation is not expected because isocyanuric acid has not absorption band in UV and VIS region.

Isocyanuric acid is low bioaccumulative (BCF < 0.5, Carp).

The potential environmental distributions of isocyanuric acid obtain from a generic Mackay level III fugacity model is shown in Table 1. Parameters used for this model are shown as Annex to this report. The results show that, if isocyanuric acid is released into water, it is unlikely to be distributed into other compartments. If isocyanuric acid is released into air and soil, it is likely to be distributed in other compartments.

Table 1
Environmental distribution of isocyanuric acid
Using a generic level III fugacity model.

Compartment	Release 100% to air	Release 100% to water	Release 100% to soil
Air	0.1 %	0.0 %	0.0 %
Water	46.5 %	99.6 %	40.5 %
Soil	53.3 %	0.0 %	59.3 %
Sediment	0.2 %	0.4 %	0.2 %

As this chemical is used in closed system as an intermediate of chemical products and is not included in consumer products, its release to the environment may occur only from the production cite.

3.1.2 Predicted Environmental Concentration

As isocyanuric acid is produced under the well-controlled closed system, amount of release to air phase is negligibly small. The waste of isocyanuric acid from the production system is released to water phase after treated its own wastewater treatment plant. Therefore, Predicted Environmental Concentration (PEC) will be calculated only for the water environment.

a. Regional exposure

According to report from a Japanese manufacturer, 407.7 tonnes/year (measured) of isocyanuric acid are released with 2.19 x 10^{10} L/year of effluent into river. Local Predicted Environmental Concentration (PEC_{local}) is calculated to be 0.186 mg/L as a worst case scenario, employing the following calculation model and dilution factor of 100.

$$\frac{\text{Amount of release } (4.08 \times 10^{11} \text{ mg/y})}{\text{Volume of effluent } (2.19 \times 10^{10} \text{ L/y}) \times \text{Dilution Factor } (100)}$$

3.2 Effects on the Environments

3.2.1 Effects on aquatic organisms

Acute and chronic toxicity data of isocyanuric acid to aquatic organisms are summarized below (Table 2). Toxicity of this chemical to aquatic organisms seems low because all toxicity data are higher than 32 mg/l (NOEC of reproduction of *Daphnia magna*). Predicted No Effect Concentration (PNEC) of this chemical was determined based mainly on the toxicity data obtained by the Environment Agency of Japan through a GLP-laboratory. Toxicity data by different organizations were few. As the lowest acute and chronic toxicity data, 96 h LC_{50} of *Oryzias latipes* and 21 d NOEC (reproduction) of *D. magna* were used, respectively (Table 2). All toxicity in Table 2 were calculated based on the nominal concentration as the measured concentrations were kept within 95 to 102 % of the nominal concentrations.

The assessment factors of 100 were used to both acute and chronic toxicity data to determine PNEC, according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects (EXCH/MANUAL/96-4-5.DOC/May 1996), because chronic toxicity data for fish was absent.

From chronic toxicity data (21 d NOEC of *Daphnia*):

PNEC = 32/100 = 0.32 mg/l

Thus, PNEC of isocyanuric acid is 0.32 mg/l.

Table 2

Acute and chronic toxicity data of isocyanuric acid to aquatic organisms at different trophic levels. The data were obtained by the Environmental Agency of Japan based on the OECD Test Guide Lines.

Species	Endpoint	Conc. (mg/l)	Remarks
Selenastrum capricornutum (algae)	Bms 72 h EC50 Bms. 72 h NOEC	620.0 62.5	a, 1) c, 1),
Daphnia magna (Water flea)	Imm 48 h EC50 Rep 21 d EC50 Rep 21 d NOEC	1000 65.9 32.0	a, 1), c, 1) c, 1), C
Oryzias latipes (fish, Medaka)	Mor 96 h LC50 Mor 14 d LC50	> 100 > 100	a, 1), A a, 1)

Notes: Bms; biomass, Mor; mortality, Rep; reproduction, NR; not recorded.
A), C); the lowest values among the acute or chronic toxicity data of algae, Cladocera (water flea) and fishes to determine PNEC of isocyanuric acid.

1) Toxicity data were obtained by the Environment Agency of Japan based on OECD Test Guidelines and GLP.

3.2.2 Terrestrial effects

No data available

3.2.3 Other effects

No data available

3.3 Initial Assessment for the Environment

Predicted No Effect Concentration (PNEC) of this chemical has been calculated as 0.32 mg/l.

PEC from Japanese local exposure scenario is 0.186 mg/l.

PEC_{local} / PNEC = 0.186/0. 32 = 0.58 < 1

Therefore, it is currently considered of low potential risk for environments and low priority for further work.

4. HUMAN HEALTH

4.1 Human Exposure

4.1.1 Occupational exposure

Isocyanuric acid is produced in a closed system and used as an intermediate for organic chemicals. The occupational exposure is expected through inhalation and the dermal route is assumed negligible because this chemical is solid. As the atmospheric concentration in plant was not measured, the maximum exposure level is estimated according to working schedules as follows. If a single worker (body weight; 70 kg, respiratory volume; 1.25 m^3/hr) is assigned to implement this operation without protection, the highest daily intake (EHE) is calculated as 0.23 mg/kg/day as the worst case. Practically, workers always wear protective gloves and respiratory protective equipment (mask) during the operation.

	Frequency Times/day	Duration hr	Working hr/day	Maximum Concentration mg/m^3	Maximum EHE mg/kg/day
Bag Filling	80	0.08	6.5	2	0.23

EHE: Estimated Human Exposure

4.1.2 Consumer exposure

Chloroisocyanurates such as sodium dichloroisocyanurate, potassium dichloroisocyanurate, sodium dichloroisocyanurate hydrate, potassium dichloroisocyanurate hydrate and trichloroisocyanuric acid have been used in sterilizing water tank, swimming pool, bathing water, and kitchen. In water, chloroisocyanurates are hydrolized to isocyanuric acid and hypochloric acid, that is the active agent (Golaszewski & Seux: 1994). The antimicrobial activity of sodium dichloroisocyanurate was evaluated against Gram negative bacteria such as *E. coli* or *Salmonella typhimurium* and against some fungi (D'Auria, *et al.*: 1989).

It is considered that the potential for exposure to pool chemicals through swallowing water and/or dermal absorption is quite high. Allen et al. (1982) reported cumulative recovery of isocyanuric acid in the urine of swimmers, 20 hr after swimming, averaging 9.8 mg. As the worst case, high performance athletes in training are known to spend up to 4 hr/day in the pool for 300 day/year and are estimated to swallow up to 60 ml/hr of pool water (Datta: 1979). In Japan, trichloroisocyanurate is mainly used in swimming pool and the average concentration of isocyanuric acid is estimated as 50 to 100 μg/ml. Based on this information, oral daily intake of isocyanuric acid for 60 kg b.w.

person is calculated as 0.17 to 0.33 mg/kg/day. Continuous-dose automated *in vitro* dermal absorption studies conducted with isocyanuric acid demonstrated minimal absorption through rat, hairless guinea pig, human, and Test skin (Moody: 1993). Total cumulative absorption of isocyanuric acid by 24 h in Test skin and human skin was 0.02 μg/cm^2 in both cases. As 1.5 m^2 of body surface is estimated for 60 kg b.w. person, the daily intake through skin is calculated as 5 μg/kg/day as the maximum value.

4.1.3 Indirect exposure via the environment

As isocyanuric acid is persistent in water and low bioaccumulative, the exposure to the general population via the environment would be possible through drinking water processed from surface water and through fish which may accumulate this chemical.

The concentration in drinking water should be estimated to be equal to PEC calculated in Section 3.1, i.e. 0.186 mg/l. The daily intake through drinking water is calculated as 6.20 x 10^{-3} mg/kg/day (2 l/day, 60 kg b.w.).

Using the maximum bioconcentration factor of 0.5 obtained by tests, the concentration of this chemical in fish can be calculated as follows:

$$PEC_{fish} = 0.186 \text{ mg/l} \times 0.5 = 9.03 \times 10^{-5} \text{ mg/g-wet}$$

As a daily intake of fish in Japan is estimated to be 90 g for 60 kg body weight person, a daily intake of this chemical will be 1.40 x 10^{-4} mg/kg/day.

4.2 Effects on Human Health

a) Acute toxicity

[SIDS data] Oral LD_{50} for isocyanuric acid was 7,700 mg/kg b.w. for rats. In inhalation study, the minimum toxic concentration was reported to be 612 mg/m^3 in rats. (Babayan and Aleksandryan: 1985) Dermal LD_{50} for isocyanuric acid was higher than 7940 mg/kg b.w. for rabbits (Toxikologische Bewertung: 1993).

Other acute toxicity information including sodium isocyanurate are given in Table. In addition, it is also reported that a single oral dosage of isocyanuric acid up to 10 g/kg was tolerated by rats and daily dosage of 20 g/kg was tolerated by rabbits for periods up to 4 days (Hodge et al.: 1965). Based on these data, isocyanuric acid is considered to be low toxic when administered as a single dose.

Routes	Strain	Type	Values	
Isocyanic acid				
Oral	Rats	LD_{50}	7,700 mg/kg	SIDS data, Ref.1
	Mice	LD_{50}	3,400 mg/kg	Ref.1
	Rabbits	LDL_0	> 10 g/kg	Ref.2
Inhalation	Rats	Other*	612 mg/m^3	SIDS data, Ref.1
Dermal	Rabbits	LD_{50}	> 7,940 mg/kg	SIDS data, Ref.3

Intravenous	Rats	LD_{50}	> 100 mg/kg	Ref.4
	Mice	LD_{50}	> 500 mg/kg	Ref.4
Sodium isocyanurate				
Oral	Rats	LD_{50}	> 7,500 mg/kg	Ref.4
Intravenous	Cats	LD_{50}	2,144 mg/kg	Ref.5

Ref.1: Babayan & Aleksandryan: 1985, Ref.2: Toxicity Information: 1972, Ref.3: Toxikologische Bewertung: 1993, Ref.4: *Gigiena i Sanitariya*: 1962, Ref.5: *J Pharmacol Exp Ther*: 1951, *: Minimum toxic concentration

b) Irritation

Federal Hazardous Substances Act (FHSA) tests of isocyanuric acid were performed in rabbits. As a result, isocyanuric acid slightly irritated to eyes but not to the skin (Hammond *et al.*: 1986). As for eye irritation, there are two other data. Moderate eye irritation followed administration into the rabbit eyes for 24 hr at 20 or 500 mg (Toxicity Information: 1972, Marhold: 1972). This chemical is not listed in IUCLID labelling and classification.

Based on these data, this chemical is considered as a slightly irritant to eyes, but not to the skin.

c) Sensitisation

There is no available data.

d) Repeated toxicity

[SIDS data] Oral toxicity study was performed in SD (Crj: CD) rats by an OECD combined repeat dose and reproductive/developmental toxicity screening test. Isocyanuric acid was administered by gavage at doses of 10, 40, 150 and 600 mg/kg/day for 45 days in males and from 14 days before mating to day 3 of lactation in females. (MHW, Japan: 1997)

Isocyanuric acid induced toxic effects at 600 mg/kg in both sexes. Excretion of reddish urine was evident. In addition, depression of body weight gain was observed in males. Urinalyses of males revealed appearance of crystals, which is considered this chemical precipitated from urine, and increases of erythrocytes and leukocytes. In hematological examination of males, significant decreases in erythrocyte counts, hemoglobin concentrations and hematocrit values were observed. In blood chemical examination of males, increases in urea nitrogen and creatinine, and a decrease of sodium were revealed. In histopathological examination, dilatation of the renal tubules, necrosis or hyperplasia of the tubular epithelium, increased basophilic tubules, neutrophilic infiltration, mineralization and fibrosis in the kidney, hyperplasia of the mucosal epithelium in the urinary bladder and vacuolization of the zona fasciculata in the adrenals were observed in both sexes. In addition, the incidence of atrophic thymus also showed a tendency for increase in females. Absolute and relative kidney weights and relative adrenal weights were increased in both sexes. As no toxic sign was observed at doses of 150 mg/kg and the less, NOAEL was considered to be 150 mg/kg/day in both sexes.

Oral toxicity study of sodium isocyanurate for 90 days was performed in B6C3F1 mice at doses of 896, 1,792 and 5,375 ppm in drinking water. Sodium hippurate was used as a second control in order

to have the sodium burden as the top concentration. Although an 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 intake. Therefore, NOAEL was considered to be 5,375 ppm (male: 1,994 mg/kg/day, female: 2,200mg/kg/day). (Hazleton: 1982)

Hodge *et al.* (1965) conducted oral toxicity study in rats and beagle dogs, and skin and eye application study in rabbits.

In first study, rats of the Rochester strain were maintained for 20 weeks on diets containing 0.8 %, and 8 % sodium isocyanurate. As a result, 14/20 males and 4/20 females died at 8 %, but no died at 0.8 %. Considerable decrease in body weight gain was observed at 8 %. Urine samples taken prior to the start of feeding and again near termination of the study showed normal concentrations of protein and sugar. In hematological examination no change was observed. There were no changes in organ weights (thyroid, liver, brain, lungs, heart, etc.), except kidney weight, which increased at 8 % in females. In histologic study, dilatation of distal collecting tubules and ducts of Bellini, with focal areas of epithelial proliferation were observed at 8 % in both sexes. Therefore, NOAEL was considered to be 0.8 % (56 mg/kg/day).

In second study, groups of 3 dogs were maintained in diets of 0.8 % sodium isocyanurate for 6 months and 8 % for 2 years. In 0.8 % dogs, 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. In 8 % group, 2 dogs died after 16 and 21 months on the regimen. 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.), except decrease in kidney weight of 2 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. Therefore, NOAEL for 6 months study was considered to be 0.8 % (291 mg/kg/day) and LOAEL for 2 years study to be 8 % (2,912 mg/kg/day).

In skin application study, 5 ml of 0.8 % or 8 % aqueous suspension were administered to the skin of albino rabbits 5 days/week for about 3 months, respectively. Urinalyses (sugar and protein) and hematological study showed no changes. 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 % sodium isocyanurate suspension, slight dilation of the ducts of Bellini and mild tubular changes were found. Therefore, NOAEL was considered to be 0.8 %.

In eye application studies, 0.1 ml of 0.8 % or 8 % aqueous suspension were administered to eye of albino rabbits 5 days/week for about 3 months, respectively. Increase in body weight was observed during the period of the study in all treated groups. No eye injury and irritation was caused. Therefore, NOAEL was considered to be 8 %.

e) Reproductive/developmental toxicity

Reproductive toxicity