lesions in the heart were also apparent in some of the highest dose males that died early. There was no evidence of a test article related carcinogenic effect. (Cascieri *et al.*: 1985)

B6C3F1 mice were administered sodium isocyanurate in drinking water at concentrations of 100, 400, 1,200 and 5,375 ppm for 2 years. Apparently swollen enlarged abdomen was observed at the highest dose groups, related to increase in water consumption. There were no effects on survival, clinical pathology (except for urinary sodium), organ weight, gross and histopathology. There was no evidence of a test article related carcinogenesis. (Industry Ad hoc Committee for Isocyanurates: 1986)

h) Toxicodynamics/toxicokinetics

Toxicokinetics study of sodium isocyanurate was performed in rats and 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 incompletely absorbed and largely eliminated in feces. The elimination half-life was 30 to 60 min in rats and 1.5 to 2 hr in dogs after oral or intravenous administration. In dogs, sodium isocyanurate distributed into an apparent volume of distribution of 0.7 L/kg, which is somewhat greater than total body water volume. Rats and 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. In rats, the remainder of radioactivity in most tissues was below the level of detection 7 days after treatment for repeated dose administration and for all sampling times for both single and repeated dose administration in dogs. As results of repeated dose study, it was shown that isocyanurate did not bioaccumulate in tissues. There was no evidence that isocyanurate was biodegraded, as only unchanged isocyanurate was found in excreta. (Barbee *et al.*: 1983)

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. This result showed that isocyanuric acid was absorbed only in very small quantities. (Toxikologische Bewertung: 1993)

i) Experience with human exposure

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 calculated as 3 hr. On the other hand, recovery of ingested isocyanuric acid was 98 % in urine. There was no correlation between toxicokinetics and gamma glutamyl transpeptidase activity. (Allen *et al.*: 1982)

4.3 Initial Assessment for Human Health

Isocyanuric acid is lowly toxic in acute toxicity studies. This chemical is considered to be slightly irritating to eyes, but not to the skin. Several subchronic oral toxicity studies demonstrated renal damages, such as dilatation of the renal tubules, necrosis or hyperplasia of the tubular epithelium, increased basophilic tubules, neutrophilic infiltration, mineralization and fibrosis. These changes were probably caused by crystal of this chemical in renal tubules. The mechanism of this renal toxicity is supported by the toxicokinetics studies in animals and humans, showing that this chemical is quickly absorbed and excreted to urine within a few hours as an unchanged form. NOAEL is considered to be 150 mg/kg/day. In a developmental toxicity study, reduction of fetal body weights and crown/rump lengths was observed and NOAEL was 200 mg/kg/day, but this most

likely reflects toxicty to the dams. No reproductive toxicity was observed (NOAEL: 600 mg/kg/day). A variety of *in vitro* and *in vivo* genotoxicity studies show this chemical is not genotoxic. Two years studies of rats and mice indicate this chemical has no carcinogenic potential.

Occupational exposure

Isocyanuric acid is used in a closed system at industries and workers wear protective gloves and respiratory protective equipment during the operation. Although the occupational exposure route is expected as an inhalation in limited workers, there is no available data of the atmosphere concentration. Based on the predicted high concentration and the possibility of exposure period, the daily intake is calculated as 0.23 mg/kg/day as the worst case. Occupational risk is presumably low because the margin of safety is 652.

Consumer exposure

Isocyanuric acid is used in the form of chlorides in sterilizing water tank, swimming pool, bathing water, and kitchen. In Japan, trichloroisocyanurate is mainly used in swimming pool and the average concentration of isocyanuric acid is estimated as 50 to 100 μg/ml. The exposure of high performance athletes in training is expected through a swallow and skin absorption. The combined daily intake is calculated as 0.34 mg/kg/day as the worst case. Consumer risk is presumably low because the margin of safety is 441.

Indirect exposure via environment

As for indirect exposure via environment, PEC_{local} of 0.186 mg/l from local exposure scenario was used for the estimation. The daily intakes through drinking water and fish were calculated as 6.20×10^{-3} mg/kg/day and 1.40×10^{-4} mg/kg/day, respectively. Since the margin of safety is very large, such as 2.42×10^{4} for drinking water and 1.08×10^{6} for fish, health risk via environment is presumably low.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Isocyanuric acid is not readily biodegradable (OECD 301C: 0 % after 14-d) and stable in water. Bioaccumulation factor of this chemical is low (BCF < 0.5, Carp). PEC/PNEC ratio (0.186/0.32 = 0.58) is less than 1 based on the local exposure scenario in the Sponsor country. It is currently considered of low potential risk to environments and low priority for further work. However, relatively high PEC/PNEC value suggests necessity for assessment of this chemical to the river ecosystem contaminated with this chemical.

Isocyanuric acid is moderately toxic in a repeated dose study (i.e. kidney) but not toxic in reproductive toxicity study. In a developmental toxicity study, this chemical is toxic to dams, which resulted in slight fetal toxicity (reduction of body weights and crown/rump lengths). This chemical is neither genotoxic nor carcinogenic but slightly irritating to eyes. Occupational and consumer risks are expected to be low because the margin of safety is 652 and 441, respectively. As the margin of safety via indirect exposure is more than 10,000, it is currently considered of low potential human risk and low priority for further work.

5.2 Recommendations

Environment: Relatively high PEC (0.18 mg/l) and PEC/PNEC ratio (0.58) in the river receiving the effluents from the production site.

Human health: No recommendation

6. REFERENCES

- Allen, M.L. *et al.*, *Drug Metab.Rev.*, 13, 499 (1982)
- Babayan, A.A. and Aleksandryan, A.V., *Zh.Eksp.Klin.Med.*, 25(4), 345 (1985)
- Barbee, S.J. *et al.*, *Toxicologist*, 3, 80 (1983)
- Cascieri, T. *et al.*, *Toxicologist*, 5, 58 (1985)
- D'Auria, F.D. *et al.*, *Ann.Ig.*, 1, 1445-1458 (1989)
- Datta, P.R., *Hazard Evaluation Division Report prepared for Special Pesticide Review Division*, p1 (1979)
- FMC Corporation, Industrial Bio Test, Report E 756 (1972)
- Gigiena i Sanitariya. For English translation, see HYSAAV. (V/O Mezhdunarodnaya Kniga, 113095 Moscow, USSR) 27(12), 13 (1962)
- Golaszewski, G. and Seux, R., *Water Res.*, 28, 207 (1994)
- Hammond, B.G. *et al.*, *Environ.Health Perspect.*,69, 287 (1986)
- Hammond, B.G. *et al.*, *Fundam.Appl.Toxicol.*, 5(4), 655 (1985)
- Hayworth, S. *et al.*, *Environmental Mutagenesis*, 5(1), 3 (1983)
- Hazleton, U.S. (Vienna), Thirteen week toxicity study in mice - Sodium monocyanurate, Report 2169-100 (1982)
- Hodge, H.C. *et al.*, *Toxicol.Appl.Pharmacol.*, 7, 667 (1965)
- Industry Ad hoc Committee for Isocyanurates, Hazleton laboratories, Report 2169-100 (1986)
- Indutry ad hoc Committee for Isocyanurates, Research Institute Int., Project 013-312-582-7 (1981a)
- Industry ad hoc committee for Isocyanurates, SRI International, Project LSC 2923, Task 1 (1981b)
- *Journal of Pharmacology and Experimental Therapeutics*, 103, 420 (1951)
- Marhold, J.V., Institut Pro Vychovu Vedoucicn Pracovniku Chemickeho Prumyclu Praha, Czechoslovakia, 152 (1972)
- Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 429-442 (1997)
- Moody, R.P., *J. Toxicol., Cutaneous Ocul. Toxicol.*, 12, 197 (1993)
- NORSOLOR/APC, Inductest performed by Institut Pasteur de Paris (M. Hofnung), Contract 133 (1977)
- Sobti,R.C. *et al.*, Cytogenetic monitoring of environmental pollutants in South Florida, AACR Abstracts, 435 (1981)
- Toxicity Information (Monsanto Industrial Chemicals Co., Bancroft Bldg., Suite 204, 3411 Silverside Rd., Wilmington, DE 19810) (1972)
- Toxikologische Bewertung. Heidelberg, Berufsgenossenschaft der chemischen Industrie, 103, 28 p (1993)
- Wheeler, A.G. *et al.*, *Toxicologist*, 5, 189 (1985)

Appendix 1

Method for Prediction of Environmental Concentration of Pollutant in Surface Water

1. Predicted environmental concentration in the local environment (PEC_{local}) with effluent release into river

When decomposition, precipitation and vaporization of pollutant can be ignored, it is used that simplified equation by complete mixing model shown with equation (1) to calculate predicted environmental concentration in the local environment (PEC_{local}) as for release effluent into river.

$$PEC_{local}\ (mg/L) = \frac{Co\ Q + Cs\ Qs}{Q + Qs} \qquad (1)$$

Where

Co: Concentration of pollutant in upper stream of release point (mg/L)
Cs: Concentration of pollutant in effluent (mg/L)
Q: Flow rate of river (m^3/day)
Qs: Flow rate of effluent released into river (m^3/ day)

At the equation (1), when Co can be considered as 0, dilution factor of pollutant in the river (R) can be shown with following equation.

$$R = Cs/C = (Q + Qs) / Qs \qquad (2)$$

As the worst case, it is used to employ a flow rate at dry season as flow rate of river (Q). When flow rate at dry season is indistinct, it is estimated using the following equation in Japan.

$$\text{Flow rate at dry season} = \text{mean flow late} / 2.5 \qquad (3)$$

2. Predicted environmental concentration in the local environment (PEC_{local}) with effluent release into sea

For prediction of concentration of pollutant in the sea water with effluent, it is employed generally Joseph-Sendnersymbol 146 ¥f "Times New Roman" ¥s 11'}s equation (4). This equation is one of analytic solution led under the following conditions from diffusion equation.

1 It is adopted large area of sea or lake.
2 The flow rate of effluent and concentration of pollutant in the effluent are constant, and distribution of concentration is able to regard as equilibrium state.
3 Effluent is distributed uniformly to vertical direction, and it spreads in a semicircle or segment to horizontal direction.
4 Diffusion coefficient of pollutant at the sea is in proportion to distance from release point of effluent.
5 There is not any effect of tidal current.
6 Decomposition of pollutant can be ignored.

$$C(x) = (C_s - C(r))\left(1 - \exp\left(-\frac{Q_s}{d\,p}\left(\frac{1}{x} - \frac{1}{r}\right)\right)\right) + C(r) \quad (4)$$

Where

C (x): Concentration of pollutant at distance x (m) from release point
Cs: Concentration of pollutant in effluent
C (r): Concentration of pollutant at distance r (m) from release point
Qs: Flow rate of effluent (m^3/day)
: Opening angle of seacoast (rad.)
d: Thickness of diffusion layer (m)
P: Diffusion velocity (m/day) (1.0 0.5 cm/sec)

When C(x) is 0 at r = and density stratification is ignored for simplification, Joseph-Sendnersymbol 146 ¥f "Times New Roman" ¥s 11'}s equation (4) is simplified to equation (5)

$$C(x) = C_s\left(1 - \exp\left(-\frac{Q_s}{d\,p\,x}\right)\right) \quad (5)$$

Because of Qs/ d p x << 1 except vicinity of release point, dilution factor in distance x from release point R(x) can be shown with equation (6).

$$R(x) = C_s/C(x) = d\,p\,x/Q_s \quad (6)$$

When it is employed following parameters in equation (6) as default, dilution factor R can be shown with equation (7).

P = 1 cm/sec (860 m/day)
= 3.14
d = 10 m
x = 1000 m

$$R = 2.7\ 10^7/Q_s \quad (7)$$

Qs: volume of effluent (m^3/day)

REVISED OECD HPV FORM 1

SIDS DOSSIER ON THE HPV PHASE 5 CHEMICAL

Isocyanuric acid

CAS No. 108-80-5

Sponsor Country: Japan

DATE: March 15, 1999

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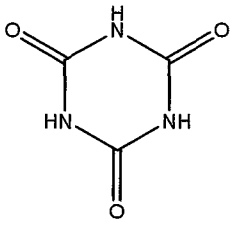
Appendix-1

Note: *; Data Elements In The Sids
†; Data Elements Specially Required For Inorganic Chemicals

SIDS PROFILE

1.01 A.	**CAS No.**	108-80-5
1.01 C.	**CHEMICAL NAME (OECD Name)**	Isocyanuric acid
1.01 D.	**CAS DESCRIPTOR**	
1.01 G.	**STRUCTURAL FORMULA**	
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	20,000 tonnes/year in Japan
1.7	**USE PATTERN**	Intermediate in closed system.
1.9	**SOURCES AND LEVELS OF EXPOSURE**	407.7 tonnes/year Release into river
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)	SIDS testing required: Water solubility, Vapour pressure, Octanol/water partition coefficient, Stability in water, Biodegradation, Chronic toxicity to daphnia, Combined repeat dose and reproductive toxicity, Chromosomal aberration test in vitro	

SIDS SUMMARY

CAS NO: 108-80-5		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL-CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.3	Density	N						N
2.4	Vapour Pressure	N						Y
2.5	Partition Coefficient	N						Y
2.6	Water Solubility	N						Y
	pH and pKa values	N						N
2.12	Oxidation: Reduction potential	N						N
OTHER P/C STUDIES RECEIVED								
ENVIRONMENTAL FATE and PATHWAY								
3.1.1	Photodegradation	N						N
3.1.2	Stability in water	N						Y
3.2	Monitoring data	N						N
3.3	Transport and Distribution	N						N
3.5	Biodegradation	N						Y
OTHER ENV FATE STUDIES RECEIVED								
ECOTOXICITY								
4.1	Acute toxicity to Fish	Y	N	N	Y	N	N	Y
4.2	Acute toxicity to Daphnia	Y	N	N	Y	N	N	Y
4.3	Toxicity to Algae	N						Y
4.5.2	Chronic toxicity to Daphnia	N						Y
4.6.1	Toxicity to Soil dwelling organisms	N						N
4.6.2	Toxicity to Terrestrial plants	N						N
4.6.3	Toxicity to Birds	N						N
OTHER ECOTOXICITY STUDIES RECEIVED								
TOXICITY								
5.1.1	Acute Oral	Y	N	N	Y	N	Y	N
5.1.2	Acute Inhalation	Y	N	N	Y	N	Y	N
5.1.3	Acute Dermal	Y	N	N	Y	N	Y	N
5.4	Repeated Dose	Y	N	Y	Y	N	Y	Y
5.5	Genetic Toxicity *in vitro*							
	. Gene mutation	Y	N	N	Y	N	Y	N
	. Chromosomal aberration	N						Y
5.6	Genetic Toxicity *in vivo*	Y	N	N	Y	N	Y	N
5.8	Reproduction Toxicity	Y	N	Y	Y	N	Y	Y
5.9	Development / Teratogenicity	Y	N	Y	Y	N	Y	N
5.11	Human experience	Y	N	N	Y	N	Y	N
OTHER TOXICITY STUDIES RECEIVED		Y	N	N	Y	N	Y	N

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

***A. CAS number** 108-80-5

B. Name *(IUPAC name)*

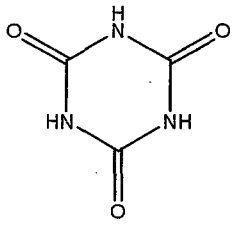
***C. Name** *(OECD name)* Isocyanuric acid

†D. CAS Descriptor

E. EINECS-Number 203-618-0

F. Molecular Formula $C_3H_3N_3O_3$

***G. Structural Formula**



H. Substance Group

I. Substance Remark

J. Molecular Weight 129.08

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:

Name of Lead Organisation: Ministry of Health and Welfare (MHW)
Ministry of International Trade and Industry (MITI)
Environmental Agency (EA)
Ministry of Labour (MOL)

Contact person: Mr. Kazuhide Ishikawa
Second International Organization Division
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C. Name of responder

Same as above contact person