Isocyanuric Acid
[108-80-5]

Review of Toxicological Literature

Prepared for

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EXECUTIVE SUMMARY

The nomination by the NIEHS of isocyanuric acid [108-80-5] to the ICCEC is based on widespread exposure of the general population through use in formulations for common household cleaners, and for swimming pool disinfection.

U.S. producers of isocyanuric acid include Israel Chemicals Ltd., Occidental Chemical Corporation, Monsanto Company, and Olin Corporation. For large-volume manufacture, isocyanuric acid is almost exclusively produced via pyrolysis of solid urea in kilns. Most of the commercially produced isocyanuric acid is chlorinated to form derivatives that are used in formulations for scouring powders, household bleaches, institutional and industrial cleansers, automatic dishwasher compounds, general sanitizers, and for swimming pool disinfection. Isocyanuric acid, at concentrations of about 25 mg/L (0.19 mM), is used in swimming pools to prevent the destruction of available chlorine by ultraviolet light. In the laboratory, isocyanuric acid is used for the production of cyanic acid. Although isocyanuric acid was at one time used as a pesticide, it is no longer a component of any registered products. Sodium isocyanurate is not produced commercially in the United States.

A 1984 survey by NIOSH concluded that 2932 workers (including 1003 female workers) among 88 plants were occupationally exposed to isocyanuric acid.

Isocyanuric acid was detected in waste water from the production of the herbicide ametryne. The degradation of simazine in corn seedlings also results in the production of isocyanuric acid. If released to soil, isocyanuric acid will be highly mobile; if released to water, it will not volatilize. In the atmosphere, isocyanuric acid will exist as both a vapor and particulate matter. In the vapor phase, it will degrade via reaction with photochemically produced hydroxyl radicals, with an estimated half-life of approximately 102 days. Wet and dry deposition act to physically remove isocyanuric acid from air. Since it absorbs UV light above 290 nm, isocyanuric acid has the potential to photolyze directly. Isocyanuric acid is readily biodegraded into carbon dioxide and ammonia by microorganisms, provided that there is no other source of nitrogen. Isocyanuric acid biodegrades particularly well in either low or zero dissolved-oxygen levels. Aquatic bioconcentration and adsorption are not thought to be significant fate processes for isocyanuric acid.

Exposure to isocyanuric acid occurs via inhalation of dusts or via skin or eye contact with the solids or powders; ingestion is not a major route of exposure.

In humans, the kinetics of isocyanuric acid excretion fit a one-compartment open model with first-order input and elimination. In rats, isocyanuric acid is rapidly excreted unchanged. In *in vitro* tests, isocyanuric acid was poorly absorbed through skin preparations. In rats and dogs, sodium isocyanurate is neither metabolized nor bioaccumulated; it is rapidly excreted unchanged.

The reported LD_{50} values for isocyanuric acid and sodium isocyanurate indicate that the compounds are slightly toxic to practically nontoxic. Application of isocyanuric acid in aqueous solution to rabbit skin caused slight to severe irritation, whereas application of isocyanuric acid in saline solution produced no irritation. Changes in kidneys were observed in rabbits following dermal application of 6.8% isocyanuric acid, or 8% sodium isocyanurate for 3 months.

Administration by gavage of a single dose of isocyanuric acid (1000-2000 mg/kg or 5000 mg/kg (7.75-15.49 mmol/kg or 38.73 mmol/kg) to rats was toxic in some animals. In another study, oral administration of a single dose of 10,000 mg/kg (77.46 mmol/kg) isocyanuric acid to rats and rabbits produced no adverse effects; administration of 4 doses of 20,000 mg/kg (154.93 mmol/kg) caused a decrease in appetite. Dystrophic changes in the kidneys were detected in rats and guinea pigs orally administered isocyanuric acid (30 mg/kg/day; 0.23 mmol/kg/day) for 6 months. No adverse effects were observed in rats and dogs fed 0.68% isocyanuric acid in the diet (50 mmol/kg feed) for 6 months or 1 year, or in rats and guinea pigs orally administered 10 mg/kg/day (0.07 mmol/kg/day) sodium isocyanurate for 6 months.

Bladder calculi accompanied with hyperplasia were detected in some male mice and rats orally administered 2000 mg/kg/day (13.15 mmol/kg/day) or 500 mg/kg/day (3.29 mmol/kg/day) sodium isocyanurate, respectively (duration of exposure not specified). Calculi in the urinary tract associated with chronic renal disease and hyperplasia were detected in mice and rats treated in the diet with 10,000, 20,000, or 30,000 ppm (65.76, 131.51, or 197.26 mmol/kg feed) (mice), or 15,000 or 30,000 ppm (98.63 or 197.26 mmol/kg feed) (rats) sodium isocyanurate for 6 to 8 months. There were no adverse effects in mice and rats administered 6000 mg/kg/day (39.45 mmol/kg/day) sodium isocyanurate by gavage for 14 weeks. Kidney damage occurred in rats and dogs administered 8% sodium isocyanurate in the diet (500 mmol/kg feed) for 5 or 6 months. Sodium isocyanurate was not carcinogenic in mice or rats administered the compound in drinking water for 24 months. Mice received 100-5375 ppm (0.66-35.34 mM); rats received 400-5375 ppm (2.63-35.34 mM). In some male rats there were pathological changes secondary to urinary tract blockage by calculi. Bladder calculi were not detected in female rats, but in some high-dose female rats there was slight tubular nephrosis.

Application of a single dose of 100 mg (0.78 mmol) isocyanuric acid to the eyes of rabbits was corrosive. In other studies, application of 20, 82, or 500 mg (0.15, 0.63, or 3.87 mmol) isocyanuric acid produced only mild ocular irritation in rabbits. No ocular damage or irritation was observed in rabbits that had 0.1 mL of an 8% sodium isocyanurate suspension applied to one eye, 5 days/week for 3 months.

There was no evidence of carcinogenicity in mice that were treated on skin daily, 3 times/week for 18 months, with 0.1 mL of an 20:1 aqueous solution of sodium isocyanurate and calcium hypochlorite. Liver tumors were detected in some mice after approximately 2 years of dermal treatment, 3 times/week, with 2 or 3 drops of isocyanuric acid in a 20% benzene solution. The significance of this occurrence is questionable because the study did not include any control animals and because benzene is itself carcinogenic. Myeloid leukosis and cysticerian sarcoma were detected in mice and rats, respectively, treated in the diet daily with 280-310 mg/kg (2.17-2.40 mmol/kg) (mice) or 150-300 mg/kg (1.16-2.32 mmol/kg) (rats) isocyanuric acid for approximately 2 years. The study did not include any control animals. There was no evidence of carcinogenicity in mice and rats treated with 300, 1000, or 3000 ppm sodium isocyanurate in the diet (1.97, 6.58, or 19.73 mmol/kg feed) for 18 (mice) or 24 (rats) months. Pulmonary lymphosarcoma and subdermal lipoma were detected in rats after 28 and 30.5 months, respectively, of once weekly subcutaneous (s.c.) treatment with 300-600 mg/kg (2.32-4.65 mmol/kg) isocyanuric acid. No tumors were

detected in mice treated s.c. once/week with 550-620 mg/kg (4.26-4.80 mmol/kg) isocyanuric acid for more than 2 years.

In a number of studies, sodium isocyanurate and isocyanuric acid were neither fetotoxic nor teratogenic in mice, rats, and rabbits.

Isocyanuric acid was found to give primarily negative results in a variety of prokaryotic and mammalian assays for genotoxicity. Isocyanuric acid, however, did induce an increase in chromatid and chromosomal aberrations in human lymphoid cells, and was reported to be incorporated into the nucleic acid of *Escherichia coli*.

No immunotoxicity data for isocyanuric acid were found.

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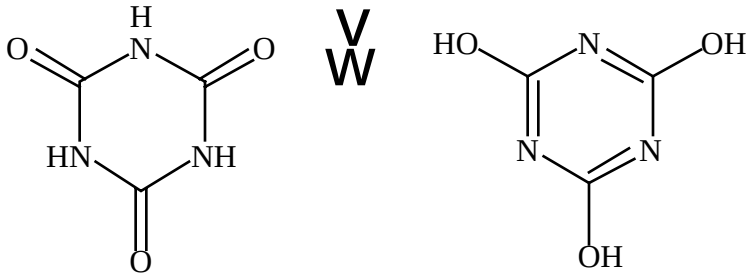
1.0 BASIS OF NOMINATION TO THE ICCEC

The nomination by the NIEHS of isocyanuric acid [108-80-5] is based on widespread exposure of the general population.

2.0 CHEMICAL PROPERTIES

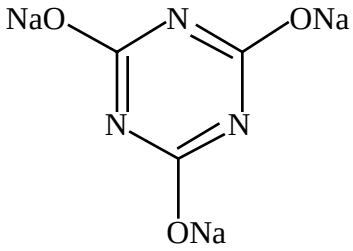
Isocyanuric acid
[108-80-5]



Isocyanuric Acid Cyanuric Acid

Tautomeric Equilibrium

Sodium Isocyanurate
[2624-17-1]



2.1 Chemical Identification

Isocyanuric acid ($C_3H_3N_3O_3$, mol. wt. = 129.08) is also called:

1,3,5-Triazine-2,4,6(1*H*,3*H*,5*H*)-trione (9CI)
s-Triazine-2,4,6(1*H*,3*H*,5*H*)-trione (8CI)
Cyanuric acid
Cyanuric acid (ACN)(VAN)
Isocyanurate acid
Pseudocyanuric acid
1,3,5-Triazine-2,4,6-triol
s-Triazine-2,4,6-triol
s-Triazinetriol (ACN)
s-2,4,6-Triazinetriol
2,4,6-Triazinetrione
s-Triazinetrione
s-Triazine-2,4,6-trione
Tricarbimide
Tricyanic acid
Trihydroxycyanidine
2,4,6-Trihydroxy-1,3,5-triazine

(Note that with the synonyms, *s*-, *S*-, and *Sym*- can be used interchangeably, sometimes S- may also be used.)

Sodium Isocyanurate ($C_3H_3N_3O_3 \cdot Na$, mol. wt. = 152.08) is also called:

Cyanuric acid, sodium derivative (6CI)
Sodium, [(4,6-dihydroxy-*s*-triazin-2-yl)oxy]- (7CI)
1,3,5-Triazine,2,4,6(1*H*,3*H*,5*H*)-trione, monosodium salt (9CI)
Acovenoside B
Cyanuric acid sodium salt (1:1)
Monosodium cyanurate
Monosodium isocyanurate
s-Triazine-2,4,6(1*H*,3*H*,5*H*)-trione, monosodium salt
Sodium isocyanurate

2.2 Physical-Chemical Properties

Isocyanuric acid

Property	Information	Reference
Color	White	Budavari (1996)
Physical State	Crystalline solid	Budavari (1996)
Melting Point, °C	Does not melt up to 330°C. Sublimes and dissociates to isocyanic acid (HNCO) at higher temperatures	Budavari (1996)
Specific Gravity at 25°C	1.75 (anhydrous)	Budavari (1996)
Dissociation Constants:		
pKa_1	6.88	Budavari (1996)
pKa_2	11.40	Budavari (1996)
pKa_3	13.5	Budavari (1996)
Odor	Odorless	Burakevich (1979)
pH, at room temperature, of an aqueous saturated solution	4.5	Burakevich (1979)

Isocyanuric acid (continued)

Property	Information	Reference
Solubility:		
Water at 25°C	Slightly soluble (0.2%)	Budavari (1996)
Organic Solvents	Slightly soluble in acetone, benzene, diethyl ether, ethanol, hexane, and isopropyl alcohol Soluble in 96% sulfuric acid, dimethyl sulfoxide, pyridine, concentrated HCl, hot alcohols, and aqueous NaOH and KOH	Budavari (1996), Burakevich (1979), and Trochimowicz et al. (1994)

Isocyanuric acid is probably not flammable (Trochimowicz et al., 1994). It reacts violently with ethanol, and will react with chlorine to form a spontaneously explosive product. When heated to decomposition, it emits very toxic NO_x and CN^- fumes (Lewis, 1992). Isocyanuric acid has a stable ring that is slowly hydrolyzed by hot aqueous alkaline solutions (Burakevich, 1979).

Sodium Isocyanurate

Property	Information	Reference
Color	colorless	Radian Corporation (1991)
Physical State	powder	Radian Corporation (1991)
Melting point, °C	>300	Radian Corporation (1991)
Solubility		
Water	Soluble in water	Radian Corporation (1991)

Sodium cyanurate has low volatility and flammability, and is stable under normal laboratory conditions. No other physical-chemical properties were found.

2.3 Commercial Products

Isocyanuric acid (98.5% pure) is generally sold coarsely granulated, minimum of approx. 85% 0.14-2 mm (-10 to 100 mesh). Its two largest bulk suppliers are FMC Corporation and the Monsanto Company (Burakevich, 1979).

3.0 PRODUCTION PROCESS

Isocyanuric acid is prepared from carbonyldiurea or from carbonyldiburet by heating, by boiling with alkalies; or by heating in excess phosgene at 150˚C (Schmidt, 1872; cited by HSDB, 1996). It is also prepared from allantoin via oxidation with hydrogen peroxide in slightly alkaline solution at 80˚C (Moore, 1917; cited by HSDB, 1996). For large-volume manufacture, isocyanuric acid is almost exclusively produced via pyrolysis of solid urea in kilns. The solid urea is heated at 200-300˚C for several hours. In the laboratory, isocyanuric acid is produced via hydrolysis of cyanuric chloride, or via acid digestion of melamine (Burakevich, 1979). Sodium isocyanurate is formed during the neutralization of cyanuric acid with sodium hydroxide (HSDB, 1996).

4.0 PRODUCTION AND IMPORT VOLUMES

U.S. producers of isocyanuric acid include Israel Chemicals Ltd., Occidental Chemical Corporation, Monsanto Company, Olin Corporation (SRI Int., 1994; Chem. Mark. Rep., 1996), and FMC Corporation (Burakevich, 1979). FMC Corporation and the Monsanto Company have produced an estimated 28,000 Mg (metric tons) (61,740,000 lb) isocyanuric acid per year (Burakevich, 1979).

Chemical Marketing Report (1996) noted that Toby's Chemical Company planned to begin production of 600 tons of merchant cyanuric acid per year at its Silver Creek, NE plant. If successful, Toby's Chemical Company planned to increase production of cyanuric acid to 5000 tons over the next 1 or 2 years.

Sodium isocyanurate is not produced commercially in the U.S. (HSDB, 1996), but it is probably transiently produced during recovery of cyanuric acid from aquatic wastes for reuse in production of trichlorocyanuric acid and/or dichloroisocyanurate salt.

5.0 USES

Most of the commercially produced isocyanuric acid is chlorinated to form derivatives that are used in formulations for scouring powders, household bleaches, institutional and industrial cleansers, automatic dishwasher compounds, general sanitizers, and for swimming pool disinfection (Burakevich, 1979). Isocyanuric acid is used in swimming pools at concentrations of about 25 mg/L (0.19 mM) to prevent the destruction of available chlorine by ultraviolet light; and in restaurants and barns for disinfection. In the laboratory, isocyanuric acid is used for the production of cyanic acid (Reinhardt and Britelli, 1981). Although isocyanuric acid was at one time used as an antimicrobial pesticide, it is no longer a component of any registered products (U.S. EPA/OPP, 1992; cited by HSDB, 1996).

6.0 ENVIRONMENTAL OCCURRENCE

6.1 Occurrence

Isocyanuric acid was detected in waste water from the production of the herbicide ametryne (Cook et al., 1983). The degradation of simazine in corn seedlings results in the production of isocyanuric acid (Gzik and Graeser, 1975). The use of isocyanuric acid in swimming pools may also result in its release to the environment (HSDB, 1996).

6.2 Persistence

If released to soil, isocyanuric acid is expected to be highly mobile; if released to water, it will not volatilize. If released to the atmosphere, isocyanuric acid will exist as both a vapor and particulate matter. In the vapor phase, it will degrade via reaction with photochemically produced hydroxyl radicals, with an estimated half-life of approximately 102 days. Wet and dry

deposition act to physically remove isocyanuric acid from air. Since it absorbs UV light above 290 nm, isocyanuric acid has the potential to photolyze directly (HSDB, 1996).

Isocyanuric acid is readily biodegraded into carbon dioxide and ammonia by microorganisms, provided that there is no other source of nitrogen (Zeyer et al., 1980, 1981; cited by Shayela et al.,1988). Isocyanuric acid biodegrades particularly well in either low or zero dissolved-oxygen levels (HSDB, 1996).

Aquatic bioconcentration and adsorption are not thought to be significant fate processes for isocyanuric acid. Based on a water solubility of 2000 mg/L (15.49 mM), the bioconcentration factor (BCF) for isocyanuric acid was estimated to be approximately 8.5. At 10 mg/L and 1 mg/L (0.08 and 0.01 mM), the BCF for isocyanuric acid was estimated to be < 0.1 and < 0.5, respectively, for a 6-week period (HSDB, 1996).

7.0 HUMAN EXPOSURE

Exposure to isocyanuric acid occurs mainly via inhalation of dusts or via skin or eye contact with the solids or powders; ingestion is not a major route of exposure (Reinhardt and Britelli, 1981). Because of its use in formulations for common household cleaners, and for swimming pool disinfection, the general population is exposed to isocyanuric acid.

7.1 Occupational Exposure

See **Table 1** for exposure by occupation, and **Table 2** for exposure by industry.

Table 1. NIOSH National Occupational Exposure Survey[a]: By Occupation

Occupation	Number of Plants	Number of Employees	Number of Female Employees
Chemical Technicians	7	1822	272

Machine Operators, not specified	6	200	17
Miscellaneous Machine Operators, N.E.C.	25	492	369
Mixing and Blending Machine Operators	25	49	
Packaging and Filling Machine Operators	25	369	345
TOTAL	—	2932	1003

[a]NIOSH (1984)
Abbreviations: N.E.C. = not elsewhere classified

Table 2. NIOSH National Occupational Exposure Survey[a]: By Industry

Industry	Number of Plants	Number of Employees	Number of Female Employees
Business Services	7	1822	272
Chemicals and Allied Products	30	1111	731
TOTAL	37	2933	1003

[a]NIOSH (1984)

7.2 Non-occupational Exposure

7.2.1 Exposure Related to Use in Swimming Pools

Pure isocyanuric acid and some of its chlorinated derivatives may be found stored at the homes of pool owners (Burakevich, 1979).

In a review by Canelli (1974), it was noted that a 50-kg person who ingests 100 mL of pool water containing 25 mg (0.19 mmol) cyanuric acid receives less than 1/100,000 of the oral LD_{50} for isocyanuric acid in rats. In a later review (Hammond et al., 1986), it was reported that a 70-kg swimmer might ingest 1 to 2 cups of pool water, which would result in a maximum exposure of 0.7 mg/kg isocyanurate, a level of exposure much lower than the no-effect level for

male rats (154-371 mg/kg). Endurance swimmers in training, known to spend up to 4 hours/day in swimming pools for up to 300 days/year, are estimated to swallow up to 60 mL/hour of pool water (Datta, 1979; cited by Moody et al., 1993). This would result in a maximum daily exposure of 0.36 mg/kg isocyanuric acid.

7.2.2 Dietary Exposure

Since the degradation of simazine in corn seedlings results in the production of isocyanuric acid (Gzik and Graeser, 1975), there is potential for exposure via consumption or processing of corn products.

8.0 REGULATORY STATUS

REGULATIONS

	Regulation	Effect of Regulation/Other Comments
EPA	40 CFR 52 Subpart O (719-740). Illinois	Isocyanuric acid appears in a table titled "List of Chemicals Defining Synthetic Organic Chemical and Polymer Manufacturing."
	40 CFR 60 Subpart VV. Standards of Performance for Equipment Leaks of VOC in the Synthetic Organic Chemicals Manufacturing Industry.	Isocyanuric acid is one of the chemicals produced by facilities covered under Subpart VV.
	40 CFR 414. Organic Chemicals, Plastics, and Synthetic Fibers.	Total cyanide (which includes isocyanuric acid) in effluent may not exceed 1200 µg/L for any one day or 420 µg/L for "any monthly."

9.0 TOXICOLOGICAL DATA

Summary: In humans, the kinetics of isocyanuric acid excretion fit a one-compartment open model with first-order input and elimination. In rats, isocyanuric acid is rapidly excreted unchanged. In *in vitro* tests, isocyanuric acid was poorly absorbed through skin preparations. In rats and dogs, sodium isocyanurate is neither metabolized nor bioaccumulated; it is rapidly excreted unchanged.

Application of isocyanuric acid in a 25% aqueous solution to rabbit skin caused slight to severe irritation, whereas application of isocyanuric acid in saline solution produced no irritation to rabbit skin. Changes in the kidneys were observed in rabbits following dermal application of 6.8% isocyanuric, or 8% sodium isocyanurate for 3 months.

The reported LD_{50} values for isocyanuric acid and sodium isocyanurate indicate that the compounds are slightly toxic to practically nontoxic. Administration by gavage of a single dose of isocyanuric acid (1000-2000 or 5000 mg/kg; 7.75-15.49 or 38.73 mmol/kg) to rats was toxic in some animals. In another study, oral administration of a single dose of 10,000 mg/kg (77.47 mmol/kg) isocyanuric acid to rats and rabbits produced no adverse effects; administration of 4 doses of 20,000 mg/kg (154.93 mmol/kg) caused a decrease in appetite. Dystrophic changes in the kidneys were detected in rats and guinea pigs orally administered isocyanuric acid (30 mg/kg/day; 0.23 mmol/kg/day) for 6 months. No adverse effects were observed in rats and dogs fed 0.68% isocyanuric acid in the diet (50 mmol/kg feed) for 6 months or 1 year, or in rats and guinea pigs orally administered 10 mg/kg/day (0.07 mmol/kg/day) sodium isocyanurate for 6 months.

Bladder calculi accompanied with hyperplasia were detected in some male mice and rats orally administered 2000 mg/kg/day (13.15 mmol/kg/day) or 500 mg/kg/day (3.29 mmol/kg/day) sodium isocyanurate, respectively (duration of exposure not specified). Calculi in the urinary tract associated with chronic renal disease and hyperplasia were detected in mice and rats treated in the diet with 10,000, 20,000, or 30,000 ppm (65.76, 131.51, or 197.26 mmol/kg feed) (mice), or 15,000 or 30,000 ppm (98.63 or 197.26 mmol/kg feed) (rats) sodium isocyanurate for 6 to 8 months. There were no adverse effects in mice and rats administered 6000 mg sodium isocyanurate/kg/day (39.45 mmol/kg/day) by gavage for 14 weeks. Kidney damage occurred in rats and dogs administered 8% sodium isocyanurate in the diet (500 mmol/kg feed) for 5 or 6 months.

Application of a single dose of finely ground 100 mg (0.78 mmol) isocyanuric acid in powder form to the conjunctival sac of rabbits was corrosive. In other studies, application of 20, 82, or 500 mg (0.15, 0.63, or 3.87 mmol) finely ground isocyanuric acid in powder form produced only mild ocular irritation in rabbits. No ocular damage or irritation was observed in rabbits that had 0.1 mL of an 8% sodium isocyanurate suspension applied to one eye, 5 days/week for 3 months.

There was no evidence of carcinogenicity in mice that were treated on skin daily, 3 times/week for 18 months, with 0.1 mL of an 20:1 aqueous solution of sodium isocyanurate and calcium hypochlorite. Liver tumors were detected in some mice after approximately 2 years of dermal treatment, 3 times/week, with 2 or 3 drops of isocyanuric acid in a 20% benzene solution. The significance of this occurrence is questionable because the study did not include any control animals and because benzene itself is carcinogenic. Myeloid leukosis and cysticerian sarcoma were detected in mice and rats, respectively, treated in the diet daily with 280-310 mg/kg (2.17-2.40 mmol/kg) (mice) or 150-300 mg/kg (1.16-2.32 mmol/kg) (rats) isocyanuric acid for approximately 2 years. The study did not include any control animals. Sodium isocyanurate was not carcinogenic in mice or rats administered the compound in drinking water for 24 months. Mice received 100-5375 ppm (0.66-35.34 mM); rats received 400-5375 ppm (2.63-35.34 mM). In some male rats there were pathological changes secondary to urinary tract blockage by calculi. Bladder calculi were not detected in female rats, but in some high-dose female rats there was slight tubular nephrosis. There was no evidence of carcinogenicity in mice and rats treated with 300, 1000, or 3000 ppm sodium isocyanurate in the diet (1.97, 6.58, or 19.73 mmol/kg feed) for 18 (mice) or 24 (rats) months. Pulmonary lymphosarcoma and subdermal lipoma were detected in rats after 28 and 30.5 months, respectively, of once weekly subcutaneous (s.c.) treatment with 300-600 mg/kg (2.32-4.65 mmol/kg) isocyanuric acid. No tumors were detected in mice treated s.c. once/week with 550-620 mg/kg (4.26-4.80 mmol/kg) isocyanuric acid for more than 2 years.

In a number of studies, sodium isocyanurate and isocyanuric acid were neither fetotoxic nor teratogenic in mice, rats, and rabbits.

Isocyanuric acid was found to give primarily negative results in a variety of prokaryotic and mammalian assays for genotoxicity. Isocyanuric acid and sodium isocyanurate did not induce *his* gene mutations in *Salmonella typhimurium*. Isocyanuric acid also did not induce an increase in sister chromatid exchanges (SCE) in human lymphoid cells, SCE in Chinese hamster ovary (CHO) cells, or *tk* gene mutations in L5178Y TK+/- mouse lymphoma cells. Monosodium cyanurate did not induce dominant lethal mutations in male albino mice or chromosome aberrations in rat bone marrow. Isocyanuric acid, however, did induce an increase in chromatid and chromosomal aberrations (structural and numerical) in human lymphoid cells, and was reported to be incorporated into the nucleic acid of *Escherichia coli*, partially replacing thymidine or uracil.

No immunotoxicity data for isocyanuric acid were found.

9.1 Human Data

There were 3 reports of ocular injury and 1 report of dermal injury from exposure to isocyanuric acid in 1987 in California (Maddy et al., 1990). The ocular injuries occurred in

residents exposed accidentally (2 cases) and in a non-use situation (1 case). The case of dermal injury occurred in a worker employed as a mixer/loader of isocyanuric acid.

9.2 General Toxicology

9.2.1 Chemical Disposition, Metabolism, and Toxicokinetics

In humans, the kinetics of isocyanuric acid excretion fit a one-compartment open model with first-order input and elimination (Allen et al., 1982). Five volunteers soaked in a swimming pool for 120 minutes. The mean urinary elimination half-life ($t_{1/2}$) was 2.2 hours, and the average recovery of isocyanuric acid from urine after 20 hours was 9.8 mg (0.076 mmol). These values represent all routes of absorption (i.e., oral and dermal) of isocyanuric acid.

In rats, isocyanuric acid is rapidly excreted unchanged (Kearney and Kaufman, 1975; cited by HSDB, 1996). *In vitro*, isocyanuric acid is poorly absorbed through the skin of Sprague-Dawley rats, hairless guinea pigs, and humans, and through artificial Testskin7® (Moody, 1993; Moody et al., 1993).

In rats and dogs, sodium isocyanurate is neither metabolized nor bioaccumulated; it is rapidly excreted unchanged (Barbee et al., 1983 abstr., 1984 abstr.; Inokuchi et al., 1978; cited by Hammond et al., 1986). When administered orally in a single dose to Sprague-Dawley rats (Barbee et al., 1983 abstr.) and dogs (strain not provided) (Barbee et al., 1984 abstr.), sodium isocyanurate was absorbed completely at a dose of 5 mg/kg (0.03 mmol/kg), but only partially at a dose of 500 mg/kg (3.29 mmol/kg). It was excreted rapidly, mainly in the urine, by both rats and dogs. The elimination $t_{1/2}$ for rats was 30-40 minutes with the low dose, and approximately 2.5 hours with the high dose. The $t_{1/2}$ for dogs was 1.5-2.0 hours for both doses. Seven days after administration of the high dose, sodium isocyanurate was detected in only trace amounts in

several tissues. No changes in the disposition of sodium isocyanurate were detected when it was administered for 15 days to rats and dogs, as compared to administration of a single dose.

9.2.2 Acute Exposures

Acute toxicity values are listed in **Table 3** for isocyanuric acid and in **Table 4** for sodium isocyanurate. Several acute toxicity studies listed in these tables failed to determine the LD_{50} because of the apparent nontoxicity of isocyanuric acid and sodium isocyanurate.

Other acute toxicity data are presented in **Table 5**.

Table 3. Acute Toxicity Values for Isocyanuric Acid

Route	Species (Strain)	LD_{50} Value mg/kg (mmol/kg)	Reference
dermal	rabbit (New Zealand white)	> 5000 (> 38.73)	Monsanto (1981)
	rabbit (strain n.p.)	> 7940 (> 61.51)	Monsanto (unpublished data; cited by Hammond et al., 1986)
i.v.	mouse (strain n.p.)	> 500 (> 3.87)	Gigiena I Sanitariya (1962; cited by RTECS, 1996)
	rat (strain n.p.)	> 100 (> 0.78)	
oral	mouse (strain n.p.)	3400 (26.34)	J. Exp. Clin. Med. (1985; cited by RTECS 1996)
	rat (Sprague-Dawley)	1510 (11.70)	Monsanto (1964)

Route	Species (Strain)	LD_{50} Value mg/kg (mmol/kg)	Reference
	rat (strain n.p.)	> 5000 (> 38.73)	Mazaev (1964; cited by Canelli, 1974)
	rat (albino)	> 5000 (> 38.73)	Monsanto (1981)
	rat (strain n.p.)	7700 (59.65)	J. Exp. Clin. Med. (1985; cited by RTECS 1996)
	rat (strain n.p.)	> 10,000 (> 77.47)	Monsanto (unpublished data; cited by Hammond et al., 1986)
		LD Value mg/kg (mmol/kg)	
oral	rabbit (strain n.p.)	> 10,000 (> 77.47)	Monsanto (year not given; cited by RTECS, 1996)
		LD_{Lo} Value mg/kg (mmol/kg)	
dermal	rabbit (New Zealand white)	> 2510 (> 19.44), and > 3980 (> 30.83)	Monsanto (1964)

Abbreviations: i.v. = intravenous; LD = lethal dose; LD_{Lo} = lowest lethal dose; n.p. = not provided

Table 4. Acute Toxicity Values for Sodium Isocyanurate

Route	Species (Strain)	LD_{50} Value mg/kg (mmol/kg)	Reference
i.v.	cat (strain n.p.)	2144 (14.10)	J. Pharmacol. Exp. Ther. (1951; cited by RTECS, 1996)
oral	rat (strain n.p.)	> 7500 (> 49.32)	Mazaev (1964; cited by Canelli, 1974)

Route	Species (Strain)	LD_{50} Value mg/kg (mmol/kg)	Reference
		LD_{Lo} Value mg/kg (mmol/kg)	
oral	rat (strain n.p.)	> 7500 (> 49.32)	Gigiena I Sanitariya (1962; cited by RTECS, 1996)

Abbreviations: i.v. = intravenous; LD_{Lo} = lowest lethal dose; n.p. = not provided

9.2.2.1 Dermal Exposure

Application of 500 mg (3.87 mmol) isocyanuric acid in 25% aqueous solution to intact and abraded skin of New Zealand white rabbits for 24 hours was corrosive (Monsanto, 1964), whereas the same dose in a saline solution applied for 24 hours to intact and abraded skin of New Zealand white rabbits produced no irritation (Monsanto, 1981). In two other also seemingly conflicting studies using New Zealand white rabbits, application of 398-3980 mg/kg acid (3.08-30.83 mmol/kg) isocyanuric acid in a 25% aqueous solution to intact skin was slightly toxic (Monsanto, 1964), whereas application of 5000 mg/kg isocyanuric acid (38.74 mmol/kg) in saline to intact and abraded skin produced no adverse effects (Monsanto, 1981). Application of the aqueous solution (dose not specified) caused marked discomfort, dyspnea, and weakness; eschar formation at the site of application and pulmonary hyperemia were also observed. The highest dose (3980 mg/kg; 30.83 mmol/kg) caused death on day 2. The other doses were not lethal.

9.2.2.2 Oral Exposure

Oral administration of a single dose of isocyanuric acid at 1000-2000 (Monsanto, 1964) or 5000 mg/kg (Monsanto, 1981) (7.75-15.49 or 38.73 mmol/kg) to Sprague Dawley rats was toxic in some animals. Signs of toxicity in rats administered 1000-2000 mg/kg (7.746-15.49

mmol/kg) included collapse followed by temporary recovery, salivation, severe diarrhea, tremors, and dyspnea (Monsanto, 1964). There was severe inflammation of the gastrointestinal tract and renal hyperemia (dose not provided). Most deaths occurred within 24 hours of dosing. Two of 10 rats

Table 5. Acute Toxicity of Isocyanuric Acid

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
9.2.2.1 Dermal Exposure						
rabbit (New Zealand white; age n.p.)	exposed: 6 rabbits (sex n.p.) controls: untreated skin served as control	isocyanuric acid, purity n.p.	500 mg (3.87 mmol) in 25% aqueous solution applied to intact and abraded skin	24 hr; rabbits were observed for several days	Isocyanuric acid was classified as corrosive on both intact and abraded skin. Dermal irritation was the only parameter evaluated.	Monsanto (1964)
rabbit (New Zealand white; age n.p.)	exposed: see Dose controls: none	isocyanuric acid, purity n.p.	398 (1 F), 631 (1 M), 1000 (1 F), 1580 (1 M), 2510 (1 F), or 3980 (1 M) mg/kg (3.08, 4.89, 7.746, 12.24, 19.44 , 30.83 mmol/kg) in 25% aqueous solution applied to intact skin	24 hr.; observation period n.p.	Signs of toxicity included marked discomfort, dyspnea, and weakness (dose n.p.). Eschar formation at the site of application and pulmonary hyperemia were also observed. The highest dose caused death on day 2. The other doses were not lethal.	
rabbit (New Zealand white; young adult)	exposed: 3 M, 3 F controls: untreated skin served as control	isocyanuric acid, purity n.p.	500 mg (3.87 mmol) ground isocyanuric acid in saline applied to 2 intact and 2 abraded sites	24 hr; rabbits were observed for 3 days following treatment	The treatment did not cause irritation of intact or abraded skin.	Monsanto (1981)
rabbit (New Zealand white; young adult)	exposed: 5 M, 5 F controls: none	isocyanuric acid, purity n.p.	5000 mg/kg (38.73 mmol/kg) in saline applied to intact and abraded skin	24 hr.; rabbits were observed for 15 days	There were no compound-related clinical or pathological changes. There were no deaths.	
9.2.2.2 Oral Exposure						
rat (Sprague-Dawley; age n.p.)	exposed: 2-3 rats/sex/ dose controls: none	isocyanuric acid, purity n.p.	1000, 1260, 1580, or 2000 mg/kg (7.746-15.49 mmol/kg) in 25% aqueous solution via gavage	single dose; observation period n.p.	Signs of toxicity included collapse followed by temporary recovery, salivation, severe diarrhea, tremors, and dyspnea. There was severe inflammation of the gastrointestinal tract and renal hyperemia (dose n.p.). Most deaths occured within 24 hours of dosing.	Monsanto (1964)

Abbreviations: F = female; M = male; n.p. = not provided

Table 5. Acute Toxicity of Isocyanuric Acid (continued)

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
rat (Sprague-Dawley; young adult)	exposed: 5 M, 5 F controls: none	isocyanuric acid; purity n.p.	5000 mg/kg (38.73 mmol/kg) in 40% aqueous solution via gavage	single dose; rats were observed for 15 days	1 M and 1 F exhibited signs of toxicity including lack of fecal material, sedation, ataxia, piloerection, urine stained fur, and porphyrin around the nose. The M also had significant body weight loss. All symptoms subsided by day 4.	Monsanto (1981)
rat (strain and age n.p.)	n.p.	isocyanuric acid; purity n.p.	10,000 or 20,000 mg/kg (77.47 or 154.93 mmol/kg)	single dose (10,000 mg/kg) or 4 doses (20,000 mg/kg) (duration of exposure n.p.); observation period n.p.	The low dose, administered once, produced no adverse effects. The high dose, administered 4 times, caused a decrease in appetite.	Clayton and Clayton (1981, 1982; cited by HSDB, 1996)
rabbit (strain and age n.p.)	n.p.	isocyanuric acid; purity n.p.	10,000 or 20,000 mg/kg (77.47 or 154.93 mmol/kg)	single dose (10,000 mg/kg) or 4 doses (20,000 mg/kg) (duration of exposure n.p.); observation period n.p.	The low dose, administered once, produced no adverse effects. The high dose, administered 4 times, caused a decrease in appetite.	
9.2.2.3 Ocular Exposure						
rabbit (New Zealand white; age n.p.)	exposed: 6 rabbits (sex n.p.) controls: untreated eye served as control	isocyanuric acid, purity n.p.	100 mg (0.78 mmol) finely ground isocyanuric acid in powder form placed into conjunctival sac of right eye	single application; eyes were either unrinsed following application or were rinsed after 2 or 4 sec. of exposure	Isocyanuric acid was classified as a corrosive eye irritant. Rabbits from all treatment groups exhibited ocular irritation.	Monsanto (1964)
rabbit (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	20 mg (0.15 mmol)	24 h; observation period n.p.	Mild irritation was produced.	Monsanto Co. (1972; cited by RTECS, 1996)
rabbit (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	500 mg (3.87 mmol)	24 h; observation period n.p.	Mild irritation was produced.	Marhold (1972; cited by RTECS, 1996)

Abbreviations:

F = female; M = male; n.p. = not provided

Table 5. Acute Toxicity of Isocyanuric Acid (continued)

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
rabbit (New Zealand white; young adult)	exposed: 3 M, 3 F controls: untreated eye served as control	isocyanuric acid; purity n.p.	82 mg (0.63 mmol) ground isocyanuric acid in powder form placed into conjunctival sac of right eye	single application [eyes were not rinsed]; rabbits were observed for 3 days.	Two females developed slight conjunctival irritation that subsided by day 2 or 3.	Monsanto (1981)

Abbreviations:

F = female; M = male; n.p. = not provided

administered 5000 mg/kg (38.73 mmol/kg) exhibited signs of toxicity including lack of fecal material, sedation, ataxia, piloerection, urine stained fur, and porphyrin around the nose (Monsanto, 1981). One animal also had significant body weight loss. All symptoms subsided by day 4.

Administration of a single dose of 10,000 mg/kg (77.47 mmol/kg) isocyanuric acid to rats and rabbits (strains and ages not provided) produced no adverse effects, but administration of 4 doses of 20,000 mg/kg (154.93 mmol/kg) isocyanuric acid to the animals caused a decrease in appetite (Clayton and Clayton, 1981, 1982; cited by HSDB, 1996). The duration of exposure to the high dose was not specified.

9.2.2.3 Ocular Exposure

Application of a single dose of finely ground 100 mg (0.78 mmol) isocyanuric acid in powder form to the conjunctival sac of New Zealand white rabbits was corrosive (Monsanto, 1964). In other studies (Marhold, 1972, and Monsanto, 1972; cited by RTECS, 1996; Monsanto, 1981), application of 20, 82, or 500 mg (0.15, 0.63, or 3.87 mmol) finely ground isocyanuric acid in powder form produced only mild ocular irritation in rabbits.

9.2.3 Short-term and Subchronic Exposures

Studies described in this section are presented in **Table 6**.

9.2.3.1 Dermal Exposure

Changes in kidneys were observed in rabbits following dermal application of 6.8% isocyanuric acid (Clayton and Clayton, 1981, 1982; cited by HSDB, 1996), or 8% sodium isocyanurate (Hodge, 1965; cited by Canelli, 1974) for 3 months. The types of changes produced by isocyanuric acid were not specified; sodium isocyanurate caused slight dilation of

the Bellini's ducts (renal tubules). Lower doses (0.68% isocyanuric acid and 0.8% sodium isocyanurate) caused no adverse effects.

9.2.3.2 Oral Exposure

Bladder calculi accompanied with bladder epithelial hyperplasia were detected in some male B6C3F1 mice administered 2000 mg/kg/day (13.15 mmol/kg/day) sodium isocyanurate, and CD rats administered 500 mg/kg/day (3.29 mmol/kg/day) sodium isocyanurate (Industry *ad hoc*

Table 6. Short-term and Subchronic Toxicity of Isocyanuric Acid and Sodium Isocyanurate

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
9.2.3.1 Dermal Exposure						
rabbit (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	0.68 or 6.8% suspension applied daily to 10% of body	3 mo; observation period n.p.	The high dose produced changes in kidneys (n.p.). The low dose caused no adverse effects.	Clayton and Clayton (1981, 1982; cited by HSDB, 1996)
rabbit (albino; age n.p.)	n.p.	sodium isocyanurate, purity n.p.	5 mL/day, 5 days/wk, of a suspension containing 0.8 or 8% sodium isocyanurate, applied to 10% of body surface	3 mo; observation period n.p.	The high dose produced no local irritation, but caused slight dilation of the Bellini's ducts (renal tubules). The low dose caused no adverse effects.	Hodge (1965; cited by Canelli, 1974)
9.2.3.2 Oral Exposure						
mouse (B6C3F1; age n.p.)	n.p.	sodium isocyanurate, purity n.p.	2000-2200 mg/kg/day (13.15-14.47 mmol/kg/day)	n.p.	Bladder calculi accompanied with bladder epithelial hyperplasia were detected in a few high-dose male mice. It was not specified whether females were also exposed.	Industry *ad hoc* Committee (unpublished observations; cited by Hammond et al., 1986)
mouse (B6C3F1; age n.p.)	n.p.	sodium isocyanurate, purity n.p.	500-6000 mg/kg/day (3.29-39.45 mmol/kg/day) by gavage [Higher doses precipitated out of solution, so it was not clear if the full dose was delivered.]	14 wk; observation period n.p.	There were no compound-related clinical effects or lesions in the tissues of high-dose mice.	NTP (private communication; cited by Hammond et al., 1986)
rat (CD; age n.p.)	n.p.	sodium isocyanurate, purity n.p.	500-700 mg/kg/day (3.29-4.60 mmol/kg/day)	n.p.	Bladder calculi accompanied with bladder epithelial hyperplasia were detected in a few high-dose male rats. It was not specified whether females were also exposed.	Industry *ad hoc* Committee (unpublished observations; cited by Hammond et al., 1986)
rat (F344; age n.p.)	n.p.	sodium isocyanurate, purity n.p.	500-6000 mg/kg/day (3.29-39.45 mmol/kg/day) by gavage [Higher doses precipitated out of solution, so it was not clear if the full dose was delivered.]	14 wk; observation period n.p.	There were no compound-related clinical effects or lesions in the tissues of high-dose rats.	NTP (private communication; cited by Hammond et al., 1986)
rat (strain and age n.p.)	exposed: 5 M controls: n.p.	isocyanuric acid, purity n.p.	trichloroisocyanuric acid in combination with isocyanuric acid (1:200 concentration ratio) in tap water [absolute concentrations n.p.]	1 mo; observation period n.p.	No adverse effects were observed.	Hodge, (1958; cited by Canelli, 1974)
9.2.3.3 Ocular Exposure						
rabbit (albino; age n.p.)	5 rabbits (sex n.p.)	sodium isocyanurate, purity n.p.	0.1 mL/day, 5 days/wk, of a suspension containing 8% sodium isocyanurate, applied to 1 eye of each rabbit	3 mo; observation period n.p.	There was no ocular damage or irritation.	Hodge (1965; cited by Canelli, 1974)

Table 6. Short-term and Subchronic Toxicity of Isocyanuric Acid and Sodium Isocyanurate

Abbreviations: M = male; n.p. = not provided

Committee, unpublished observations; cited by Hammond et al., 1986). Lower doses caused no adverse effects in the mice and rats. The study was described as subchronic in the review by Hammond et al. (1986), although the actual duration of exposure was not given.

There were no compound-related clinical effects or lesions in the tissues of B6C3F1 mice and F344 rats administered 500-6000 mg/kg/day (3.29-39.45 mmol/kg/day) sodium isocyanurate by gavage for 14 weeks (NTP, private communication; cited by Hammond et al., 1986).

Administration of trichloroisocyanuric acid in combination with isocyanuric acid (1:200 concentration ratio; absolute concentrations not given) in tap water to male rats (strain and age not specified) for 1 month had no effect on the incidence of organ abnormalities in offspring (Hodge, 1958; cited by Canelli, 1974).

9.2.3.3 Ocular Exposure

No ocular damage or irritation was observed in albino rabbits that had 0.1 mL of an 8% sodium isocyanurate suspension applied to one eye, 5 days/week for 3 months (Hodge, 1965; cited by Canelli, 1974).

9.2.4 Chronic Exposures

Studies described in this section are presented in **Table 7**.

In some studies, chronic exposure to isocyanuric acid or sodium isocyanurate caused changes in the urinary tract. Dystrophic changes in kidneys were detected in rats and guinea pigs (strains and ages not specified) orally administered isocyanuric acid at a dose of 30 mg/kg/day (0.23 mmol/kg/day) for 6 months (Mazaev, 1962, 1964; cited by Canelli, 1974). A lower dose of 3.0 mg/kg/day (0.02 mmol/kg/day) produced no adverse effects in the animals.

Calculi in the urinary tract associated with chronic renal disease and hyperplasia of the bladder mucosa were detected in mice and rats (strains and ages not specified) administered

sodium isocyanurate in the diet for 6 to 8 months (Laveglia et al., 1977 abstr.). Mice received 10,000, 20,000, or 30,000 ppm sodium isocyanurate in the diet (65.76, 131.51, or 197.26 mmol/kg feed); rats received 15,000 or 30,000 ppm in the diet (98.63 or 197.26 mmol/kg feed).

Kidney damage was also observed in rats and dogs (strains and ages not specified) administered 8% sodium isocyanurate in the diet (500 mmol/kg feed) for 20 weeks (rats) or 6 months (dogs) (Hodge et al., 1965; cited by Canelli, 1974). A lower dose (0.8%; 50 mmol/kg feed) produced no adverse effects in the animals.

Table 7. Chronic Toxicity of Isocyanuric Acid and Sodium Isocyanurate

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
mouse (strain and age n.p.)	n.p.	sodium isocyanurate, purity n.p.	10,000, 20,000, or 30,000 ppm in diet (65.76, 131.51, or 197.26 mmol/kg feed)	6-8 mo; observation period n.p.	Mice in all treatment groups had calculi in the urinary tract which were associated with chronic renal disease. Degenerative changes in the kidney and hyperplasia of the bladder mucosa were also detected. Morbidity and mortality were increased after 6-8 months.	Laveglia et al. (1977 abstr.)
rat (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	3.0 or 30 mg/kg/day (0.02 or 0.23 mmol/kg/day)	6 mo; observation period n.p.	The high dose produced dystrophic changes in kidneys.	Mazaev (1962, 1964; cited by Canelli, 1974)
rat (strain and age n.p.)	n.p	sodium isocyanurate, purity n.p.	10 mg/kg/day (0.07 mmol/kg/day)	6 mo; observation period n.p.	No adverse effects were observed.	Mazaev (1962, 1964; cited by Canelli, 1974)
rat (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	0.68% in diet (50 mmol/kg feed)	6 mo; observation period n.p.	No adverse effects were observed.	Clayton and Clayton (1981, 1982; cited by HSDB, 1996)
rat (strain and age n.p.)	exposed: 20 M, 20 F per dose controls: n.p.	sodium isocyanurate, purity n.p.	0.8 or 8% in diet (50 or 500 mmol/kg feed)	20 wk; observation period n.p.	The high dose produced histological changes in the kidneys: Distal collecting tubules and Bellini's ducts were dilated with focal areas of epithelial proliferation. The low dose had no adverse effects. In the high-dose group, 14/20 M and 4/20 F died during treatment. None of the low-dose animals died.	Hodge et al. (1965; cited by Canelli, 1974)
rat (strain and age n.p.)	n.p.	sodium isocyanurate, purity n.p.	15,000 or 30,000 ppm in diet (98.63 or 197.26 mmol/kg feed)	6-8 mo; observation period n.p.	Rats in all treatment groups had calculi in the urinary tract which were associated with chronic renal disease. Degenerative changes in the kidney and hyperplasia of the bladder mucosa were also detected. Morbidity and mortality were increased after 6-8 months.	Laveglia et al. (1977 abstr.)
guinea pig (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	3.0 or 30 mg/kg/day (0.02 or 0.23 mmol/kg/day)	6 mo; observation period n.p.	The high dose produced dystrophic changes in kidneys.	Mazaev (1962, 1964; cited by Canelli, 1974)
guinea pig (strain and age n.p.)	n.p.	sodium isocyanurate, purity n.p.	10 mg/kg/day (0.07 mmol/kg/day)	6 mo; observation period n.p.	No adverse effects were observed.	Mazaev (1962, 1964; cited by Canelli, 1974)
dog (strain and age n.p.)	n.p.	isocyanuric acid, purity n.p.	0.68% in diet (50 mmol/kg feed)	6 mo or 1 yr; observation period n.p.	No adverse effects were observed.	Clayton and Clayton (1981, 1982; cited by HSDB, 1996)
dog (strain and age n.p.)	exposed: 3 (sex n.p.) per dose controls: n.p.	sodium isocyanurate, purity n.p.	0.8 or 8% in diet (50 or 500 mmol/kg feed)	6 mo (low dose) or 2 yr (high dose); surviving animals were killed at end of treatment period	In the 2 dogs that died during treatment with the high dose, kidney fibrosis, focal dilation, and epithelial proliferation of Bellini's ducts were observed. In the dog that was killed after 2 years of high-dose treatment, similar renal changes were observed, along with atrophy of the thyroid, with lymphocytic infiltration, but no hyperplasia. In the high-dose group, 14/20 M and 4/20 F died during treatment. None of the low-dose animals died.	Hodge et al. (1965; cited by Canelli, 1974)

Abbreviations: F = female; M = male; n.p. = not provided

Table 7. Chronic Toxicity of Isocyanuric Acid and Sodium Isocyanurate

Abbreviations: F = female; M = male; n.p. = not provided

No adverse effects were observed in rats and dogs (strains and ages not specified) fed 0.68% isocyanuric acid in the diet (50 mmol/kg feed) for 6 months (rats and dogs) or 1 year (dogs) (Clayton and Clayton, 1981, 1982; cited by HSDB, 1996), or in rats and guinea pigs (strains and ages not specified) orally administered 10 mg sodium isocyanurate/kg/day (0.07 mmol/kg/day) for 6 months (Mazaev, 1962, 1964; cited by Canelli, 1974).

9.3 Reproduction and Teratology

Studies described in this section are presented in **Table 8**.

9.3.1 Dermal Exposure

No teratogenic effects were observed in offspring of mice (strain and age not specified) administered 500 mg/kg (3.29 mmol/kg) sodium isocyanurate, either alone or in a 20:1 mixture with calcium hypochlorite (Laveglia et al., 1977 abstr.). The duration of exposure was not specified.

9.3.2 Oral Exposure

No teratogenic or fetotoxic effects were evident at 20 days of gestation in the fetuses of female rats administered sodium isocyanurate orally at a dose of 200-5000 mg/kg/day (1.31-32.88 mmol/kg/day) during gestation days 6-15 (Haley, 1972a, 1972b; cited by Canelli, 1974; Cascieri et al., 1983 abstr.).

In a three-generation study, there was no evidence of teratogenicity or fetotoxicity in offspring of CD rats administered 400, 1200, or 5375 ppm sodium isocyanurate in drinking water (2.63, 7.89, or 35.34 mM) for 100 or 120 days (Wheeler et al., 1985 abstr.; Hammond et al., 1986). Neither microscopic nor macroscopic changes were observed in low- or mid-dose rats. In

a few high-dose rats (generation not specified), however, urinary bladder calculi accompanied by microscopic evidence of hyperplasia or chronic cystitis were detected.

There was also no evidence of teratogenicity or fetotoxicity in offspring of Dutch belted rabbits administered sodium isocyanurate at a dose of 50, 200, or 500 mg/kg/day (0.33, 1.31, or 3.29 mmol/kg/day) via gavage on gestation days 6-18 (FMC Corporation, unpublished data; cited by Hammond et al., 1986).

Table 8. Reproduction and Teratology

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
9.3.1 Dermal Exposure						
mouse (strain and age n.p.)	n.p.	sodium isocyanurate alone or 20:1 mixture of sodium isocyanurate + calcium hypochlorite, purity n.p.	500 mg sodium isocyanurate/kg (3.29 mmol/kg)	n.p.	Neither sodium isocyanurate alone nor the 20:1 mixture was teratogenic. No other details were given.	Laveglia et al. (1977 abstr.)
9.3.2 Oral Exposure						
rat (pregnant albino; age n.p.)	exposed: 19 F per group controls: 19 F	sodium isocyanurate, purity n.p.	500 mg/kg/day (3.29 mmol/kg/day) in water, with or without 36 mg calcium hypochlorite via gavage	treatment occurred on gestation days 6-15; all dams were killed on gestation day 20	In the mice fetuses, there was no adverse effect observed between exposed and control animals.	Haley, (1972a, 1972b; cited by Canelli, 1974)
rat (pregnant; strain and age n.p.)	exposed: 25 F per dose controls: 50 F (sodium controls); 25 F (vehicle controls); 25 F (untreated)	sodium isocyanurate, purity n.p.	200, 1000, or 5000 mg/kg/day (1.31, 6.58, or 32.88 mmol/kg/day) via gavage	treatment occurred on gestation days 6-15; fetuses were removed from dams on gestation day 20	There were no adverse effects in dams or in their fetuses.	Cascieri et al. (1983 abstr.)
rat (CD; 36-day-old)	exposed: 12 M, 24 F per dose controls: 12 M, 24 F (sodium controls); 12 M, 24 F (vehicle controls)	sodium isocyanurate, purity n.p.	400, 1200, or 5375 ppm in drinking water (2.63, 7.89, or 35.34 mM)	Rats were treated for 100 days and were then mated twice to produce 2 litters (F_{1a}, F_{1b}). Weanlings from F_{1b} litter were treated for 120 days and were then mated twice to produce 2 litters (F_{2a}, F_{2b}). Weanlings from F_{2b} litter were treated for 120 days and mater once (F_{3a} litter). Some F_{3a} rats were treated for an additional 4 wk. and were then killed.	The doses were not toxic and there was no evidence of dose-related or cross-generational changes in gestation length, litter size, pup survival to weaning, sex ratio, or pup weight. No microscopic or macroscopic changes were observed in LD or MD rats. In a few HD rats (generation n.p.) urinary bladder calculi accompanied by microscopic evidence of hyperplasia or chronic cystitis were detected.	Wheeler et al. (1985 abstr.); Hammond et al, (1986)

Abbreviations: F = female(s); HD = high dose; LD = low dose; M = male(s); MD = mid dose; n.p. = not provided

Table 8. Reproduction and Teratology (continued)

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/Observation Period	Results/Comments	Reference
rabbit (pregnant Dutch belted; age n.p.)	exposed: 9-10 F (LD); 9-10 F (MD); 20-21 F (HD) controls: 20-21 F	sodium isocyanurate, purity n.p.	50, 200, or 500 mg/kg/day (0.33, 1.31, or 3.29 mmol/kg/day) via gavage	treatment occurred on gestation days 6-18; rabbits were examined on gestation day 28	There were no adverse reactions in exposed dams and there was no evidence of dose-related fetotoxicity or teratogenicity. There was no difference in mean number of live fetuses/dam or in sex ratio between groups.	FMC Corp. (unpublished data; cited by Hammond et al., 1986)

Abbreviations: F = female(s); HD = high dose; LD = low dose; M = male(s); MD = mid dose; n.p. = not provided

9.4 Carcinogenicity

Cumulative tumorigenic doses are listed below in **Table 9** for isocyanuric acid. Cumulative tumorigenic doses were not available for sodium isocyanurate. Other carcinogenicity data are presented in **Table 10**.

9.4.1 Dermal Exposure

Liver tumors were detected in some mice (strain and age not specified) after approximately 2 years of dermal treatment, 3 times/week, with 2 or 3 drops of isocyanuric acid in a 20% benzene solution (Pliss and Zabezhinskii, 1970; Pliss and Zabezhinskii, 1970; cited by Canelli, 1974). The significance of this occurrence is questionable because the study did not include any control animals and because benzene itself is carcinogenic.

There was no evidence of carcinogenicity in mice (strain and age not specified) that were treated on skin daily, 3 times/week for 18 months, with 0.1 mL of an 20:1 aqueous solution of sodium isocyanurate and calcium hypochlorite (Laveglia et al., 1977 abstr.). Sodium isocyanurate was not administered alone to any mice.

9.4.2 Oral Exposure

Myeloid leukosis and cysticerian sarcoma were detected in mice and rats (strains and ages not specified), respectively (Pliss and Zabezhinskii, 1970; Canelli, 1974). The mice were treated in the diet daily with 280-310 mg/kg (2.17-2.40 mmol/kg) isocyanuric acid, the rats with 150-300 mg/kg (1.16-2.32 mmol/kg). Myeloid leukosis was first detected in mice 23 months after the beginning of treatment. Cysticerian sarcoma was first detected in rats during month 19. The study did not include any control animals.

Sodium isocyanurate was not carcinogenic in male or female B6C3F1 mice or CD rats (ages not specified) administered the compound in drinking water for 24 months (Cascieri et al.,

1985 abstr.; Industry *ad hoc* Committee, unpublished observations; cited by Hammond et al., 1986). Mice received 100, 400, 1200, or 5375 ppm (0.66, 2.63, 7.89, or 35.34 mM) sodium isocyanurate; rats received 400, 1200, 2400, or 5375 ppm (2.63, 7.89, 15.78, or 35.34 mM) sodium isocyanurate. In some male rats that died and in some male rats that were sacrificed at 12 months, there were pathological changes secondary to urinary tract blockage by calculi, including hyperplasia, bleeding and inflammation of the bladder epithelium, dilated and inflamed ureters, and

Table 9. Cumulative Tumorigenic Doses of Isocyanuric Acid[1]

Route	Species (Strain)	Cumulative TD Value[2] mg/kg (mmol/kg)	Duration of Exposure	Tumor Location	Reference
dermal	mouse (strain n.p.)	138,000 (1069)	2 yr	liver	Voprosy Onkologii (1970; cited by RTECS, 1996)
		Cumulative TD_{Lo} Value[2] mg/kg (mmol/kg)			
oral	mouse (strain n.p.)	130,000 (1007)	2 yr	blood	Voprosy Onkologii (1970; cited by RTECS, 1996)
	rat (strain n.p.)	55,000 (426)	82 wk	liver, and skin and/or appendages	Voprosy Onkologii (1970; cited by RTECS, 1996)
s.c.	rat (strain n.p.)	27,000 (209)	2 yr	respiratory tract and blood	Voprosy Onkologii (1970; cited by RTECS, 1996)

Abbreviations: n.p. = not provided; s.c. = subcutaneous; TD = toxic dose causing a significant increase in tumor incidence; TD_{Lo} = lowest toxic dose causing a significant increase in tumor incidence

[1] All of the results in this table were labeled as "equivocal" in the RTECS review, but the reason was not provided.

[2] The cumulative dose is the total dose administered during the specified exposure period; dosing schedules were not provided by RTECS.

Table 10. Carcinogenicity of Isocyanuric Acid and Sodium Isocyanurate

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
9.4.1 Dermal Exposure						
mouse (strain and age n.p.)	exposed: 50 (sex n.p.) controls: none	isocyanuric acid, purity n.p.	2 or 3 drops of a 20% solution in benzene applied 3 times/wk	≥ 25 mo exposure	Liver tumors (1 cavernous hemangioma; 1 adenoma) were detected in two surviving rats during months 23 and 25. At the time of the first tumor appearance (mo. 23), 8 mice had survived. Cause of death was n.p.	Pliss and Zabezhinskii (1970); Canelli (1974)
mouse (strain and age n.p.)	n.p.	20:1 aqueous solution of sodium isocyanurate + calcium hypochlorite, purity n.p.	0.1 mL/day, 3 times/wk (site of application n.p.)	18 mo exposure	There was no evidence of chronic toxicity or carcinogenicity.	Laveglia et al. (1977 abstr.)
9.4.2 Oral Exposure						
mouse and rat (strain and age n.p.)	exposed: 50 (sex n.p.) per group [it was not clear if a group was defined by species or by dose] controls: none	isocyanuric acid, purity n.p.	280-310 mg/kg b.w./day (mice [(2.17-2.40 mmol/kg/day]) or 150-300 mg/kg b.w./day (rats [1.16-2.32 mmol/kg/ day]), in diet, 5 days/wk	≥ 25 mo exposure	Mouse: Two cases of myeloid leukosis were detected in the 23rd month. The dose administered to affected mice was not provided. Rat: Cysticerian sarcoma was detected in the 19th month in one and in 4 more rats between 21.5 and 25 months. Fibroadenoma of the mammary gland was detected in 2 females (latent period n.s.; these tumors were thought to be spontaneous).	Pliss and Zabezhinskii (1970); Canelli (1974)
mouse (B6C3F1; age n.p.)	exposed: 80-100 animals/sex/dose controls: 80-100 animals/sex (vehicle controls); 80-100 animals/ sex (sodium controls)	sodium isocyanurate, purity n.p.	100, 400, 1200, or 5375 ppm in drinking water (0.657, 2.63, 7.891, or 35.34 mM)	24 mo; [sacrifices were made at 6, 12, 18, and 24 mo]	The review by Hammond et al. (1986) noted that there were no treatment-related effects at any time during the 24-month study. There was no dose-related mortality.	Cascieri et al. (1985 abstr.); Industry *ad hoc* Committee (unpublished observations; cited by Hammond et al., 1986)

Abbreviations: n.p. = not provided

Table 10. Carcinogenicity of Isocyanuric Acid and Sodium Isocyanurate (continued)

Species, Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
rat (CD; age n.p.)	exposed: 80-100 animals/sex/dose controls: 80-100 animals/sex (vehicle controls); 80-100 animals/sex (sodium controls)	sodium isocyanurate, purity n.p.	400, 1200, 2400, or 5375 ppm in drinking water (2.63, 7.891, 15.78, or 35.34 mM)	24 mo; [sacrifices were made at 6, 12, 18, and 24 mo]	Hyperplasia, bleeding and inflammation of the bladder epithelium, dilated and inflamed ureters, and renal tubular nephrosis; inflammatory lesions of the heart were also observed. In some high-dose female rats, slight tubular nephrosis was detected during the first 12 mo. No bladder calculi were found in these rats. During the first 12 mo. of the study, there were treatment-related deaths of some (13/100) high-dose males caused by presence of calculi in urinary tract. During the second 12 mo., there was no treatment-related mortality.	Cascieri et al. (1985 abstr.); Industry *ad hoc* Committee (unpublished observations; cited by Hammond et al., 1986)
mouse (strain and age n.p.)	n.p.	sodium isocyanurate, purity n.p.	300, 1000, or 3000 ppm in diet (1.97, 6.575, or 19.73 mmol/kg feed)	18 mo exposure	There was no evidence of chronic toxicity or carcinogenicity.	Laveglia et al. (1977 abstr.)
rat (strain and age n.p.)	n.p.	sodium isocyanurate, purity n.p.	300, 1000, or 3000 ppm in diet (1.97, 6.575, or 19.73 mmol/kg feed)	24 mo exposure	There was no evidence of chronic toxicity or carcinogenicity.	
9.4.3 Subcutaneous Injection						
mouse and rat (strain and age n.p.)	exposed: 50 (sex n.p.) per group [it was not clear if a group was defined by species or by dose] controls: none	isocyanuric acid, purity n.p.	550-620 mg/kg (mice [4.26-4.80 mmol/kg]) or 300-600 mg/kg (rats [2.32-4.65 mmol/kg]) in sunflower oil, once/wk	≥ 30.5 mo exposure	Mouse: No tumors were detected. Rat: One case of pulmonary lymphosarcoma was detected in a survivor during month 28. A subdermal lipoma was detected in a survivor 30.5 months after the first treatment. It was not clear if the 2 tumors were detected in the same animal. At the time of the first tumor appearance (mo. 28), 5 rats had survived. Cause of death was n.p.	Pliss and Zabezhinskii (1970); Canelli (1974)

Abbreviations: n.p. = not provided

renal tubular nephrosis. In some male rats that died early, inflammatory lesions of the heart were also observed. Bladder calculi were not detected in female rats, but in some high-dose female rats there was slight tubular nephrosis.

There was no evidence of carcinogenicity in mice and rats (strains and ages not specified) treated with 300, 1000, or 3000 ppm sodium isocyanurate in the diet (1.97, 6.58, or 19.73 mmol/kg feed) for 18 (mice) or 24 (rats) months (Laveglia et al., 1977 abstr.).

9.4.3 Subcutaneous Injection

Pulmonary lymphosarcoma and subdermal lipoma were detected in rats after 28 and 30.5 months, respectively, of once weekly s.c. treatment with 300-600 mg/kg isocyanuric acid (2.32-4.65 mmol/kg) in sunflower oil (Pliss and Zabezhinskii, 1970; Canelli, 1974). No tumors were detected in mice (strain and age not specified) treated s.c. once/week with 550-620 mg/kg (4.26-4.80 mmol/kg) isocyanuric acid in sunflower oil for more than 2 years (Pliss and Zabezhinskii, 1970; Canelli, 1974). The studies did not include any control animals.

9.5 Genotoxicity

Studies described in this section are presented in **Table 11**.

9.5.1 Prokaryotic Systems

The triple auxotroph *E. coli* strain 15 arg-, thy-, ura- was exposed to 14 µg/mL (110 µM) [^{14}C]isocyanuric acid for 4 hours in the absence of S9 (Temperli et al., 1966). Following exposure, cells were washed with 95% ethanol, the DNA and RNA extracted, and the incorporated radioactivity measured using a liquid scintillation counter. The authors concluded that isocyanuric acid was incorporated into the nucleic acid of *Escherichia coli*, partially replacing thymidine or uracil.

As reported by Lusby et al. (1979), isocyanuric acid did not induce *his* gene mutations in *Salmonella typhimurium*. Strains TA98, TA100, TA1535, and TA1538 were exposed (dose levels

not provided) using the plate incorporation method in both the presence or absence of rat liver metabolic activation.

Likewise, Haworth et al. (1983) found that isocyanuric acid did not induce *his* gene mutations in *S. typhimurium*. Strains TA98, TA100, TA1535, and TA1537 were exposed to doses ranging from 100 to 10,000 µg/plate (0.78 to 77.47 µmol/plate) using the pre-incubation

Table 11. Genotoxicity of Isocyanuric Acid and Sodium Isocyanurate

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form, Purity	Dose	Endpoint Response	Comments	Reference
9.5.1 Prokaryotic Systems							
Escherichia coli strain 15 arg-, thy-, ura-	incorporation into nucleic acids	-	isocyanuric acid, n.p.	14 µg/mL (110 µM) [^{14}C]isocyanuric acid for 4 h	positive	Isocyanuric acid was reported by the authors to be incorporated into DNA and RNA, partially replacing thymidine and uracil, respectively. Following exposure, cells were washed with 95% ethanol, the nucleic acid extracted, and the incorporated radioactivity measured on a scintillation counter.	Temperli et al. (1966)
Salmonella typhimurium strains TA100, TA98, TA1535, and TA1538	his reverse gene mutations	-/+	isocyanuric acid, n.p.	n.g.	negative/negative	No other experimental details were given.	Lusby et al. (1979)
S. typhimurium strains TA100, TA98, TA97, TA1535, and TA1537	his reverse gene mutations	-/+ rat or hamster	isocyanuric acid, n.p.	100 to 10,000 µg/plate (0.78 to 77.47 µmol/plate) via the pre-incubation method	negative/negative	No increase in mutations or toxicity were observed at any dose or strain.	Haworth et al. (1983)
S. typhimurium strains TA100, TA98, TA1535, and TA1537	his reverse gene mutations	-/+	sodium isocyanurate, n.p.	10 to 10,000 µg/plate (0.08 to 77.47 µmol/plate) via the plate incorporation method	negative/negative	No increase in mutations or toxicity were observed at any dose or strain.	Hammond et al. (1985)
9.5.2 In Vitro Mammalian Genotoxicity Assays							
9.5.2.1 DNA Damage							
Human lymphoid cell line LAZ-007	Sister chromatid exchanges (SCE)	-	isocyanuric acid, n.p.	2 µg/mL (15 µM) for 48 h	negative	No other experimental details were provided.	Sobti et al. (1981 abstr.)
Chinese hamster ovary (CHO) cells	SCE	-/+	sodium isocyanurate, n.p.	94 to 1500 µg/mL (730 to 11,620 µM) for 24 h -S9 and 2 h +S9	negative/negative	Concentrations at 1000 µg/mL (7747 µM) and above were suspensions. 100 cells were analyzed per treatment for SCE.	Hammond et al. (1985)
9.5.2.2 Gene Mutations							
L5178Y TK +/- mouse lymphoma cells	tk gene mutations	-/+	sodium isocyanurate, n.p.	250 to 2000 µg/mL (1940 to 15,490 µM) for 4 h	negative/negative	Concentrations at 1000 µg/mL (7747 µM) and above were suspensions. .	Hammond et al. (1985)
9.5.2.3 Chromosomal Damage							

Abbreviations: n.p. = purity not provided; n.g. = doses not given

Table 11. Genotoxicity of Isocyanuric Acid and Sodium Isocyanurate (continued)

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form, Purity	Dose	Endpoint Response	Comments	Reference
Human lymphoid cell line LAZ-007	chromosomal aberrations	-	isocyanuric acid, n.p.	2 µg/mL (15 µM) for 48 h	positive	There was an increase in chromatid and chromosomal aberrations (structural and numerical). No effect on cell cycle was observed when compared to controls.	Sobti at al. (1981 abstr.)
9.5.3 In Vivo Mammalian Genotoxicity Assays							
9.5.3.1 Dominant Lethal Mutations							
mouse (male albino)	dominant lethal mutations	NA	isocyanuric acid, n.p.	250 mg/kg (1.94 mmol/kg) i.p. [single injection]; males were mated with 3 untreated virgin females/male/week for 6 weeks, and were sacrificed at the end of the mating period	negative	No significant increase in mutation rates was observed in the test group when compared to the control group. There was no difference in the number of implantation and resporption sites in females 1 week after the end of the mating period.	Arnold (1972; cited by Canelli, 1974)
9.5.3.2 Chromosomal Damage							
rat (male Sprague-Dawley)	chromosomal aberrations	NA	isocyanuric acid, n.p.	1250, 2500, and 5000 mg/kg (9.68, 19.37, and 38.74 mmol/kg) via gavage and sacrificed 24 and 48 h later	negative	Fifty bone marrow metaphases were examined per animal.	Hammond et al. (1985)

Abbreviations: n.p. = purity not provided; n.g. = doses not given

method in either the presence or absence of 10% rat or hamster liver metabolic activation. No increase in mutations or toxicity was observed at any dose or in any strain.

Hammond et al. (1985) similarly reported that the sodium salt of isocyanuric acid did not induce *his* gene mutations in *S. typhimurium*. Salmonella strains TA98, TA100, TA1535, and TA1537 were exposed to doses ranging from 10 to 10,000 µg/plate (0.08 to 77.47 µmol/plate) monosodium cyanurate using the plate incorporation method in both the presence or absence of rat liver metabolic activation. No mutations or toxicity was observed at any dose level in any strain.

9.5.2 *In Vitro* Mammalian Genotoxicity Assays

9.5.2.1DNA Damage

Sobti et al. (1981 abstr.) reported that isocyanuric acid did not induce an increase in sister chromatid exchanges (SCE) in human lymphoid cells. Cell line LAZ-007 was exposed to 2 µg/mL (15 µM) isocyanuric acid for 48 hours without added metabolic activation. Sodium isocyanurate also did not induce SCE in Chinese hamster ovary (CHO) cells (Hammond et al., 1985). Cells were exposed for 24 hours in the absence of S9 and for 2 hours in the presence of rat liver S9 to doses ranging from 94 to 1500 µg/mL (730 to 11,620 µM) sodium isocyanurate. Concentrations of 1000 µg/mL (7747 µM) or more were administered as suspensions. One hundred cells were analyzed per treatment level for SCE.

9.5.2.2Gene Mutations

Hammond et al. (1985) found that isocyanuric acid did not induce *tk* gene mutations in L5178Y TK+/- mouse lymphoma cells. Cells were exposed for 4 hours in the absence or presence of rat liver S9 to doses ranging from 250 to 2000 µg/mL (1940 to 15,490 µM) monosodium cyanurate. Concentrations at 1000 µg/mL (7747 µM) or greater were suspensions.

9.5.2.3 Chromosomal Damage

Sobti et al. (1981 abstr.) reported that isocyanuric acid induced an increase in chromosomal aberrations (structural and numerical) in human lymphoid cells. Cell line LAZ-007 was exposed to 2 µg/mL (15 µM) isocyanuric acid for 48 hours. No effect on cell cycle was observed.

9.5.3 *In Vivo* Mammalian Genotoxicity Assays

9.5.3.1 Dominant Lethal Mutations

Sodium isocyanurate did not induce dominant lethal mutations in male albino mice (Arnold, 1972; cited by Canelli, 1974). Animals were injected once i.p. with 250 mg/kg (1.94 mmol/kg) sodium isocyanurate with or without 16.8 mg of calcium hypochloride, and were mated with 3 untreated virgin female mice/male/week for 6 consecutive weeks. Males were sacrificed at the end of the 6-week mating period; females were sacrificed 1 week after removal from the cage containing the males. There was no difference in the number of implantation and resporption sites in females.

9.5.3.2 Chromosomal Damage

Hammond et al. (1985) found that sodium isocyanurate did not induce chromosome aberrations in bone marrow cells of male Sprague-Dawley rats given a single oral dose of 1250, 2500, and 5000 mg/kg (9.68, 19.37, and 38.74 mmol/kg) and sacrificed 24 or 48 hours later. A total of 50 metaphase cells per animal were examined.

9.6 Immunotoxicity

No data were found.

10.0 STRUCTURE-ACTIVITY RELATIONSHIPS

No data were found.

11.0 ONLINE DATABASES AND SECONDARY REFERENCES

11.1 Online Databases

Chemical Information System Files

SANSS (Structure and Nomenclature Search System)
TSCATS (Toxic Substances Control Act Test Submissions)

Internet Databases

Code of Federal Regulations full text. 1996 versions of various titles via GPO Gate, a gateway by the Libraries of the University of California to the GPO Access service of the Government Printing Office, Washington, DC. Internet URL http://www.gpo.ucop.edu/

National Library of Medicine Databases

EMIC and EMICBACK (Environmental Mutagen Information Center)

STN International Files

BIOSIS (Biological Abstracts)
CA File (Chemical Abstracts)
CANCERLIT
CEN (Chemical & Engineering News)
CIN (Chemical Industry Notes)
CSNB (Chemical Safety News Base)
EMBASE (Excerpta Medica)
HSDB (Hazardous Substances Data Bank)
IPA (International Pharmaceutical Abstracts)
MEDLINE (Index Medicus)
PROMT (Predicasts Overview of Markets and Technology)
RTECS (Registry of Toxic Effects of Chemical Substances)
TOXLINE
TOXLIT

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicology Research Projects	CRISP
NIOSHTIC7	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	ANEUPL
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA

Federal Research in Progress	FEDRIP
Developmental and Reproductive Toxicology	DART

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