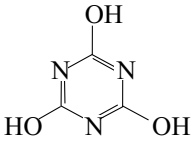
ISOCYANURIC ACID

Document History
Published: 1991
Revised: 2005
Rebranded: 2025

I. IDENTIFICATION[1,2]

Chemical Name: Isocyanuric Acid
Synonyms: Cyanuric Acid: s-Triazine-2,4,6-triol;
CAS Number: 108–80–5
Molecular Formula: $C_3H_3N_3O_3$
Structural Formula: Cyanuric acid



II. CHEMICAL AND PHYSICAL PROPERTIES[1-3]

Physical State: White crystalline powder
Molecular Weight: 129.08
Odor Description: Practically odorless
Vapor Pressure: $< 4 \times 10^{-4}$ mmHg
Saturated vapor concentration: < 0.05 ppm
Melting Point: 320°–330°C (608°F) (sublimes)
Decomposition Temperature: Decomposes at temperatures exceeding 360°C (680°F)
Conversion Factors: 1 ppm (v/v) = 5.3 mg/m³;
1 mg/m³ = 0.19 ppm
Flammability Limits: explosive vapor/air mixtures may be formed at temperatures above 320°–360°C.
Specific Gravity: 2.50 at 20°C (68°F) anhydrous; 1.768 at 20°C (68°F) dihydrate
Solubility: 2.7 g/L at 25°C (77°F)
pH: 3.6–4.0 (saturated solution) at 25°C (77°F)
pKa Dissociation Constant: 7.2
Log Pow: 0.61 (estimated)
Stability: Normally stable in dry form at room temperature. Will off-gas when wet.
Reactivity: Will decompose with trace amounts of water, steam, or acids to produce isocyanic acid (NCOH) or ammonia.
Incompatibilities: Water, ethanol, chlorine, or concentrated acids

III. USES[1,2]

Isocyanuric acid is used as an intermediate in the production of chlorinated bleaches and water treatment chemicals, as a selective herbicide, and in the manufacture of melamine.

IV. TOXICITY DATA

A. Acute Toxicity

1. Oral Toxicity

Rat: $LD_{50} > 10$ g/kg[4]
$LD_{50} = 7.7$ g/kg[5]
Mouse: $LD_{50} = 3.4$ g/kg[5]
Rabbit: $LD_{50} > 20$ g/kg[3]

2. Eye Irritation

Rabbit: Instillation with 20 mg for 24 hours caused slight irritation.[4] Instillation with 500 mg for 24 hours caused marked irritation.[6]

3. Skin

a. Absorption

Rabbit: $LD_{50} > 7940$ mg/kg[4]

Isocyanuric acid was minimally absorbed through rat, hairless guinea pig, and human skin *in vitro*.[7] The total absorption in human skin over the 24-hour exposure period was 0.02 µg/cm².

b. Irritation

Undiluted isocyanuric acid was nonirritating when applied to rabbit skin.[4]

c. Sensitization

No data available.

4. Inhalation Toxicity

Rat: Minimum toxic concentration = 612 mg/m³ as an aerosol; exposure duration not reported.[5]

B. Mutagenicity

Isocyanuric acid and sodium cyanurate were not mutagenic in replicate Ames (*Salmonella typhimurium*) microsomal assays when tested in strains TA98, TA100, TA1535, and TA1537 with and without activation at levels up to 10,000 µg per plate.[8-10]

Isocyanuric acid was not mutagenic in the mouse lymphoma forward gene mutation assay at TK-locus of L5178Y mice at concentrations up to 2000 µg/mL.[8]

No increases in sister chromatic exchange were observed in Chinese hamster ovary (CHO) cells at concentrations up to 1500 µg/mL.[8]

Isocyanuric acid was not mutagenic by *in vivo* cytogenetics (chromosomal aberrations in rat bone marrow) at single doses up to 5000 mg/kg by gavage, and was negative both with and without metabolic activation in an *in vitro* chromosomal aberration test conducted with Chinese hamster lung cells.[8,11]

C. Metabolism and Pharmacokinetics

^{14}C labeled isocyanuric acid was readily absorbed from the gastrointestinal tract following oral dosing in rats, and excreted primarily in the urine, with lesser amounts in the feces, directly dependent on the dose. No acid was observed in the expired air. No metabolites were detected. Only traces of ^{14}C were found in any tissue.[12, 13]

Isocyanuric acid given orally to dogs and rats did not bioaccumulate in the tissues and was not biotransformed.[14, 15]

Labeled sodium cyanurate was administered orally to rats at single doses of 5 and 500 mg/kg, and intravenously at levels of 5 mg/kg. At the low dose, the material was completely absorbed and excreted through the urine as the parent compound. At the higher dose, the half-life was 2.5 hours and a portion of the dose was eliminated in the feces.[16]

D. Reproductive/Developmental Toxicity

Groups of 25 pregnant CD rats were administered sodium isocyanurate by oral gavage during Days 6 to 15 of gestation at levels of 0, 200, 1000, and 5000 mg/kg/day. No mortality, weight change, or adverse reactions were observed in any of the dose groups. There was no evidence of fetotoxicity or teratogenicity.[17]

Groups of 10 pregnant Dutch belted rabbits were given sodium isocyanurate by gavage during Days 6 to 18 of gestation. Dosages of 0, 50, 200, and 500 mg/kg/day were used. No compound-related mortality, fetotoxicity, or teratogenicity was observed.[18] In a second study utilizing a similar treatment protocol and species, decreased maternal weight gain occurred at the 200 mg/kg dose level and above; this effect was reversed after the dosing period ended, however. Slight reductions in fetal size and weight were noted at the high dose level. No treatment-related fetal effects were noted at the mid- and low-dose levels, and no teratogenic effects were observed at any dose level. This study established a no observable adverse effect level (NOAEL) of 50 mg/kg/day for maternal toxicity and a NOAEL for 200 mg/kg/day for fetal toxicity.[19]

A three-generation reproduction study using sodium isocyanurate in drinking water at concentrations of 0, 400, 1200, and 5375 ppm based on cyanuric acid content was conducted in male and female CD rats. This was equivalent to dosages of 28, 84, and 370 mg/kg for males and 47, 141, and 634 mg/kg for females. The high dose level was at the limit of solubility. No compound-related mortality or reproductive toxicity was observed in any of the offspring. No significant differences in fertility index, length of gestation, litter size, or pup survival were observed at any dose level. Slight increases in male mean body weight and male urinary calculi production were seen in the high-dose group.[20]

In a combined repeat-dose and reproductive/developmental toxicity screening study, groups of 10 male and female Sprague-Dawley rats were administered 0, 10, 40, 150, or 600 mg/kg/day of isocyanuric acid by gavage. Males were treated for a total of 44 days and females were treated from 14 days prior to mating until Day 3 of lactation. Adverse effects occurred in the parental generation at the 600 mg/kg/day dose level and were related to excretion of urine saturated with test material (see subchronic toxicity section for additional information). No treatment-related differences were noted in reproductive parameters, including fertility index, gestation length, numbers of copora lutea or implantations, and behavior at delivery and lactation. There were no significant differences between control and treated pups in number, sex ratio, live birth index, viability index and body weight. No external or visceral abnormalities were observed in pups at any dose level. The no observable effect level (NOEL) for both reproductive and developmental toxicity was 600 mg/kg/day.[11]

E. Subchronic Toxicity

In a combined repeat-dose and reproductive/developmental toxicity screening study, groups of 10 male and female Sprague-Dawley rats were administered 0, 10, 40, 150 or 600 mg/kg/day of isocyanuric acid in sesame oil by gavage. Males were treated for a total of 44 days and females were treated from 14 days prior to mating until Day 3 of lactation. Urinalysis detected crystals of test material, in addition to increased numbers of erythrocytes and leukocytes in both males and females at the 600 mg/kg/day dose level. Absolute and relative kidney weights and relative adrenal weights increased in this group. Decreased erythrocyte counts, hemoglobin concentrations and hematocrits were also noted. Dilatation of renal tubules, necrosis, or hyperplasia of the tubular epithelium, mineralization and fibrosis of the kidney, hyperplasia of the mucosal epithelium in the urinary bladder, and vacuolization of the adrenals were noted in histopathological examination. The NOEL for systemic effects was 150 mg/kg/day for both males and females.[11]

Sodium isocyanurate was administered to B6C3F1 mice in drinking water for a period of 90 days at levels of 0, 400, 1200, and 5375 ppm. This was equivalent to a dose of 2000 to 2200 mg/kg at the high dose level. No adverse health effects were observed at any of the dosage levels.[21]

Groups of 10 and 20 male and female CD rats were fed 0%, 0.8% or 8.0% sodium isocyanurate, respectively, for 20 weeks; calculations of dose received were not included in the study report.[22] No adverse effects were observed at the lower dose level. Body weights at the high dose were significantly decreased in both sexes. Fourteen of the 20 males at this dose level died during the study. Relative kidney weights increased in females. Abnormal renal histopathology was noted in both sexes, including dilatation of the distal collecting tubules with areas of focal epithelial proliferation.

In a related study, groups of 3 beagle dogs (2 males and 1 female) received dietary concentrations of 0% or 0.8% (approximately 291 mg/kg/day) sodium cyanurate for 6 months, while another group received dietary concentrations, which were gradually increased over a period of several weeks to 8% sodium cyanurate (approximately 2912 mg/kg/day) for 2 years. Body weight, hematological parameters, urinalysis, organ weight, and histopathology were similar among the low-dose and control groups following 6 months of treatment. At the 8% dose level, 2 dogs died after 16 and 21 months of treatment, respectively, from undetermined causes. Body weights, hematologic parameters, and urinalysis in these dogs were similar to historical controls (concurrent controls were not included in the 2-year study). Decreased red blood cell counts, hemoglobin concentration and hematocrits were noted in the surviving dog, and decreased kidney weights were noted in the 2 dogs that survived longer than 20 months. Extensive kidney fibrosis was noted on gross and histopathological examination of these two animals. Focal areas of thyroid atrophy without evidence of hyperplasia was noted in the dog that survived to study termination.[22]

Aqueous suspensions (100 µL) containing 0.8% to 8.0% sodium isocyanurate were applied to rabbit eyes 5 days/week for 3 months. One eye was treated and one served as a control. No injury was observed. Aqueous suspension (5 mL) containing 0.8% to 8.0% sodium isocyanurate was applied to rabbit skin 5 days/week for 3 months. No irritation or other adverse effects on the skin were observed.[22]

F. Chronic Toxicity and Carcinogenicity

A 2-year carcinogenicity study was conducted in CD rats. Sodium isocyanurate was administered in the drinking water to 80 to 100 animals of each sex per group at levels of 0, 400, 1200, 2400, and 5375 ppm sodium isocyanurate. No evidence of a cyanurate-related carcinogenic effect was observed in any tissues or organs from male or female rats at any dose level.[23] Treatment-related mortality was observed in the 5375 ppm male group during the first 12 months of treatment. Death was caused by uremia resulting from urethral blockage due to formation of urinary calculi. During the last 12 months, no treatment-related mortality occurred. Hemorrhaging and inflammation of the bladder epithelium as well as renal necrosis were also observed in the high-dose animals. Physical irritation resulting from the urinary calculi was thought to be the cause of these effects. This study established NOAELs of 2400 ppm or 154 mg/kg/day for males and 266 mg/kg/day for females.

A 2-year carcinogenicity study was also conducted in B6C3F1 mice. Groups of 80 to 100 mice of each sex per concentration level were administered sodium isocyanurate in drinking water at levels of 0, 100, 400, 1200, and 5375 ppm. In both sexes at the highest dose, effects secondary to test material precipitation in the urine were noted and included mechanical irritation and physical obstruction in the urinary tract. A slight reduction in body weight was observed in high-dose

females. No evidence of a cyanurate-related carcinogenic effect was observed at any dose level. The LOAEL for systemic effects is 5375 ppm and the NOAEL is 1200 ppm. [24]

Isocyanuric acid was applied subcutaneously once per week at 60 mg/dose for Rappolov strain rats and 10 mg/dose for CC_{57} strain mice for 2 years. It was also administered orally 5 times per week at 30 mg/dose to mice for 2 years. This Russian study reported that cyanuric acid has a low carcinogenic potential. Limitations of this study include the use of non-standard animal strains and methodology, and a lack of controls.[25]

V. HUMAN USE AND EXPERIENCE

A study was conducted to quantify absorption of cyanuric acid by a group of 5 male swimmers while soaking for 120 minutes in a swimming pool containing up to 30 ppm cyanuric acid in water, or drinking an aqueous solution of cyanuric acid (concentration not reported).[26] The elimination half-life as estimated from excreta was approximately 3 hours, with 98% of the oral dose recovered within 24 hours post-exposure. The cumulative excretion of cyanuric acid ranged from 0.03 to 2.8 mg.

VI. RATIONALE

Isocyanuric acid is of low acute toxicity by the dermal and ingestion routes of exposure, is a slight skin irritant, and a slight to moderate eye irritant. It is readily absorbed following ingestion and is excreted primarily in the urine. When administered at high oral dose levels, isocyanuric acid saturates the urine and forms crystals, which cause adverse kidney and urinary tract effects; secondary hematological effects signaling excessive red blood cell loss also occur. However, these effects are not seen at lower dose levels; the NOEL for these effects is 150 mg/kg/day in both male and female rats. The available data suggest that isocyanuric acid is not mutagenic or carcinogenic and is not a reproductive or developmental toxicant.

Occupational exposure to isocyanuric acid would most likely occur by inhalation of aerosols and by dermal contact. The basis for establishing the OEL for this relatively low toxicity chemical is avoidance of the renal effects seen at very high exposure levels and maintenance of good industrial hygiene practice. No irritation threshold data upon which to base a STEL are available. Isocyanuric acid does not meet the criteria for either a skin, or dermal or respiratory sensitization notation.

VII. RECOMMENDED OEL GUIDE

8-hour time-weighted average (TWA); 10 mg/m^3, total; 5 mg/m^3, respirable.

VIII. REFERENCES

1. **Syracuse Research Corporation:** *PhysProp Database: Cyanuric acid* (CAS No. 000108–80–5). http://esc.syrres.com/interkow/webprop.exe.
2. **Windholz, M., ed.:** *The Merck Index: An Encyclopedia of Chemicals and Drugs*, 12th ed. Rahway, N.J.: Merck & Co., 1996. p. 454.
3. **Occidental Chemical Corporation:** "Material Data Safety Sheet for Cyanuric Acid, Dry." 2003. Occidental Chemical Corporation, 5005 LBJ Freeway, P.O. Box 809050, Dallas, TX 75380-9050.
4. **Monsanto Co.:** *Acute Toxicity Screen with Cyanuric Acid.* 1974. Monsanto Co., 800 N. Lindberg Blvd., St. Louis, MO 63167.
5. **Babayan, A.A., and A.V. Aleksandryan:** Title Unknown: data taken from a summary of the article in a database search. Translated from *Zh. Ekap. Klin. Med. 25(4)*:345–349 (1985).
6. **Marhold, J.V.:** Translated from Sbomik Vysledku Toxicologickeho Vysetreni Latek. Institute Pro Vychovu Vedoucicn Pracovniku Chemickeno Prumyclu, Praha, Cz., 1972. [Czechoslovakian]. As cited in: OECD SIDS Initial Assessment Report for 9th SIAM. Isocyanuric acid. p.255. March 30, 1999.
7. **Moody, R.P., B. Nadeau, S. MacDonald, and I. Chu:** *In Vitro* Skin Absorption of Carbon-14 Cyanuric Acid in a Simulated Swimming Pool. *Bull. Environ. Contam. Toxicol. 50(1)*:12–18 (1993).
8. **Hammond, B.G., S.J. Barbee, A.G. Wheeler, and T. Cascieri**: Absence of Mutagenic Activity for Monosodium Cyanurate. *Fund. Appl. Toxicol. 5(4)*:655–664 (1985).
9. **Lusby, A.F., Z. Simmons, and P.M. McGuire**: Variation in Mutagenicity of S-triazine Compounds Tested on Four Salmonella Strains. Environ. Mutagen. 1:287–290 (1979).
10. H**aworth, S, T. Lawlor, K. Mortelmans, W. Speck, and E. Zeiger.** (1983). Salmonella mutagenicity test results for 250 chemicals. *Environ. Mutagenesis Suppl*. *1*:3–142
11. **Japanese Ministry of Health and Welfare (1997)**. Toxicity Testing Reports of Environmental Chemicals. *Isocyanuric acid. 5*:429–442. wwwdb.mhlw.go.jp/ginc/cgi-bin/db1_ls1.pl
12. **Mackellar, D.G., and G.L. Kennedy:** Cyanuric Acid: Absorption, Distribution and Excretion

Studies with 14-C Labelled Cyanuric Acid (s-Triazine trione) in Rats. FMC Industrial Chemical Division Internal Report presented at Society of Toxicology meeting on March 14, 1978.

13. **Mackellar, D.G., and G.L. Kennedy:** Cyanuric Acid: Absorption, Distribution and Excretion Studies with 14-C Labelled Cyanuric Acid in Rats. *Toxicol. Appl. Pharmacol. 45*:239–242 (1978) (abstract).
14. **Inokuchi, N., R. Sawamura, A. Hasegawa, and G. Urakuro:** Distribution, Percutaneous Absorption and Excretion of Isocyanuric Acid. *Eisei Kagaki*. *24*:49–59 (1978).
15. **Barbee, S.J., T. Cascieri, B.G. Hammond, T. Inoue, N. Ishida, A.G. Wheeler, and J.L. Schardein:** Metabolism and Disposition of Sodium Cyanurate in the Dog. Abstract in *The Toxicologist 4(1)*:92 (1984).
16. **Barbee, S.J., T. Cascieri, T. Inoue, N. Ishida, A.G. Wheeler, M. Chadwick, D. Hayes, J. McCauley, and A. McCommish:** Metabolism and Disposition of Sodium Cyanurate. Abstract in *The Toxicologist 3(1)*:80 (1983).
17. **Cascieri, T., S.J. Barbee, B.G. Hammond, T. Inoue, N. Ishida, A.G. Wheeler, and J.L. Schardein:** Absence of a Teratogenic Response in Rats with Monosodium Cyanurate. Abstract in *The Toxicologist 3(1)*:65 (1983).
18. **FMC Corporation:** "Industry Report: Teratology, Monosodium Cyanurate (Rabbit)." 1974.
19. **Fisons Chemical Co.:** "Report Submitted to Industry Ad Hoc Committee on Isocyanurates." 1979. Fisons Chemical Co., 12 Darby Road, Loughborough, Leicestershire, LE11 OEB, England.
20. **Wheeler, A.G., S.J. Barbee, B.G. Hammond, T. Inoue, N. Ishida, J.L. Schardein, and T. Cascieri:** Three Generation Reproduction Study in Rats Administered Monosodium Cyanurate. Abstract in *The Toxicologist 5(1)*:189 (1985).
21. **Hazelton Laboratories American, Inc.:** "Thirteen Week Drinking Water Study in the Mouse with Monosodium Cyanurate." 1982. [Submission to the Industry Ad Hoc Committee on Isocyanurates]. Monsanto Co., 600 N. Lindberg Blvd., St. Louis, MO 63167. As cited in OECD SIDS: SIDS Initial Assessment Report for Ninth Siam. 1999.
22. **Hodge, H.C. and B.J. Panner:** Toxicity of Sodium Cyanurate. *Toxicol Appl. Pharmacol. 7*:667–674 (1965).
23. **Cascieri, T., S.J. Barbee, B.G. Hammond, T. Inoue, N. Ishida, and A.G. Wheeler:** Comprehensive Evaluation of the Urinary Tract after Chronic Exposure to Cyanurate in Drinking Water. Abstract in *The Toxicologist 5(1)*:58 (1985).
24. **Hazelton Laboratories American, Inc.:** "104 Week Oncogenicity Study with Monosodium Cyanurate in Mice." 1986. [Submission to the Industry Ad Hoc Committee on Isocyanurates]. Monsanto Co., 600 N. Lindberg Blvd., St. Louis, MO 63167. As cited in OECD SIDS: SIDS Initial Assessment Report for Ninth Siam. 1999.
25. **Pliss, G.B., and M.A. Zabezhinsky:** On Carcinogenic Properties of S-triazine Derivatives." *Vopr. Onkol. 16(1)*:82–85 (1970).
26. **Allen, L.M., T.V. Briggle, and C.D. Pfaffenberger.** (1982). Absorption and excretion of cyanuric acid in long-distance swimmers. *Drug Metabolism Reviews 13*:499–516. As cited in: OECD SIDS Initial Assessment Report for 9th SIAM. Isocyanuric acid. p.268. March 30, 1999.