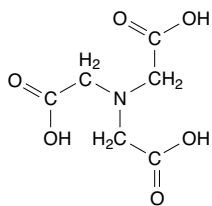


## Nitrilotriacetic Acid

### CAS No. 139-13-9

Reasonably anticipated to be a human carcinogen

First listed in the *Third Annual Report on Carcinogens* (1983)



### Carcinogenicity

Nitrilotriacetic acid is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

#### Cancer Studies in Experimental Animals

Oral exposure to nitrilotriacetic acid caused urinary-tract tumors in mice and rats. Mice and rats of both sexes were administered nitrilotriacetic acid in the diet, both as the free acid and as the trisodium salt, and male rats were administered the trisodium salt in drinking water. These exposures increased the incidences of benign or malignant tumors of the kidney, ureter, and urinary bladder; tumor types observed included tubular-cell adenoma and adenocarcinoma of the kidney and transitional-cell carcinoma of the kidney, ureter, and urinary bladder. Exposure to the free acid caused benign and/or malignant kidney tumors in mice of both sexes and in male rats, cancer of the ureter in male rats, and cancer of the urinary-bladder in female rats. Exposure to the trisodium salt had the same effects in rats and also caused kidney tumors and cancer of the ureter in female rats (NCI 1977, Goyer *et al.* 1981).

#### Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to nitrilotriacetic acid.

### Properties

Nitrilotriacetic acid is a tertiary amino-polycarboxylic acid chelating agent that exists as a white crystalline powder at room temperature (HSDB 2009, NCI 1977). It is slightly soluble in water and deuterated dimethyl sulfoxide, soluble in ethanol, and insoluble in most other organic solvents. It forms water-soluble complexes with many metals and reacts with strong oxidizing compounds (IARC 1990). Physical and chemical properties of nitrilotriacetic acid are listed in the following table.

| Property                         | Information                                   |
|----------------------------------|---|
| Molecular weight                 | 191.1 <sup>a</sup>                            |
| Specific gravity                 | > 1 at 20°C (solid) <sup>a</sup>              |
| Melting point                    | 242°C decomposes <sup>a</sup>                 |
| Log $K_{ow}$                     | -3.81 <sup>b</sup>                            |
| Water solubility                 | 59 g/L at 25°C <sup>a</sup>                   |
| Vapor pressure                   | $7 \times 10^{-9}$ mm Hg at 25°C <sup>b</sup> |
| Dissociation constant ( $pK_a$ ) | 3.03 at 20°C <sup>b</sup>                     |

Sources:<sup>a</sup>HSDB 2009, <sup>b</sup>ChemIDplus 2009.

### Use

Nitrilotriacetic acid has many commercial applications, but is used primarily as a metal ion chelating agent and as a laundry detergent builder (IARC 1990). It sequesters magnesium and calcium ions present in hard water, thereby reducing buildup and scaling caused by salts of these ions. In the late 1960s, nitrilotriacetic acid generally replaced phosphates in commercial detergents (NCI 1977). The use of nitrilotriacetic acid in detergents was suspended in the United States in 1971, but was resumed in the 1980s after phosphates were banned from detergents (HSDB 2009). Nitrilotriacetic acid also is used as an eluting agent in the purification of rare-earth elements, as a boiler feed water additive, in water and textile treatment, in metal plating and cleaning, and in pulp and paper processing (NCI 1977, IARC 1990). To a lesser extent, it is used in leather tanning, photographic development, synthetic rubber production, pharmaceutical manufacturing, and agricultural herbicide formulations and micronutrient solutions (NCI 1977). It has also been evaluated as a soil additive in the phytoremediation of heavy-metal-contaminated soil (Evangelou *et al.* 2007); chelation of the metals with nitrilotriacetic acid mobilizes them for more rapid uptake by plants.

### Production

Nitrilotriacetic acid was first synthesized in 1862, and commercial production began in Europe in the 1930s (IARC 1990). In 1970, before its use in detergents was suspended, 150 million pounds of nitrilotriacetic acid was produced and used in the United States, of which 86% to 92% was used in detergents (NCI 1977). In the early 1980s, most of the annual U.S. production (approximately 66 million pounds) was exported (IARC 1990). In 2009, nitrilotriacetic acid was produced by 17 manufacturers worldwide, but none in the United States (SRI 2009), and was available from 31 suppliers, including 13 U.S. suppliers (ChemSources 2009). No current data on U.S. imports or exports of nitrilotriacetic acid were found. Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of nitrilotriacetic acid totaled 500,000 lb to 1 million pounds in 1986 and 1998, 1 million to 10 million pounds in 1990, and 10,000 to 500,000 lb in 1994 and 2000 (EPA 2004).

### Exposure

The routes of potential human exposure to nitrilotriacetic acid are inhalation, ingestion, and dermal contact (HSDB 2009). The general population may be exposed through ingestion of drinking water or dermal contact with products containing nitrilotriacetic acid or its salts. Assessments of exposure to nitrilotriacetic acid were conducted in the United States in 1979, 1980, and 1985 and in Canada in 1996. These surveys assessed exposure from drinking water, bathing, wearing clothing washed with detergents containing nitrilotriacetic acid, contacting wash water, and ingesting residues remaining on hand-washed dishes. All of these studies concluded that the total daily exposure to consumers from all sources was less than 1 µg/kg of body weight per day (IARC 1999).

In 1988, EPA's Toxics Release Inventory reported environmental releases of 13,000 lb of nitrilotriacetic acid, of which 20% was released to air, 40% to surface water, and 40% to on-site landfills (TRI 2009). From 1988 to 1996, annual releases declined to a low of 1,600 lb. Since 1999, releases have ranged from 2,900 lb in 2000 to almost 64,000 lb in 2007, released by four industrial facilities. Most of the 2007 releases were to landfills, but almost 2,500 lb was released to an underground injection well.

When released to air, nitrilotriacetic acid will exist mostly in particulate form and will be removed by wet and dry deposition (HSDB

## Report on Carcinogens, Twelfth Edition (2011)

2009). In surface water, it will not volatilize or bioaccumulate in aquatic organisms; it will exist in ionized form and will likely remain in the water until biodegradation occurs, with a half-life of 0.34 to 15 days. Mean concentrations of nitrilotriacetic acid in surface water ranged from less than 0.5 to 6.4 mg/L in German rivers and lakes (Schmidt *et al.* 2004). In Canada, typical concentrations in ground and drinking water were 1 to 5 µg/L, and concentrations in Canadian environmental water samples ranged from 0.006 to 3.2 mg/L (Rakshit 2002). In Canada and Switzerland, nitrilotriacetic acid makes up about 15% of laundry detergents; the load in raw wastewater was measured at 2,500 µg/L in Canada and 100 to 1,000 µg/L in Switzerland (Bucheli-Witschel and Egli 2001). In well-adapted activated sludge systems, nitrilotriacetic acid is readily biodegraded. In soil, it is likely to biodegrade under aerobic conditions and moderate temperatures (HSDB 2009).

Occupational exposure to nitrilotriacetic acid may occur through inhalation and dermal contact during the manufacture of the compound or its salts, during water treatment, and during other procedures in which nitrilotriacetic acid is used. The National Occupational Hazard Survey (conducted from 1972 to 1974) estimated that 13,454 workers potentially were exposed to nitrilotriacetic acid, trisodium salt (NIOSH 1976). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 25,216 workers potentially were exposed to nitrilotriacetic acid and 249,479 workers potentially were exposed to its trisodium salt (NIOSH 1990). In 1990, it was estimated that approximately 2,600 workers potentially were exposed to nitrilotriacetic acid salts during production and detergent formulation; the potential for exposure was highest for workers loading hopper cars (IARC 1990).

## Regulations

### Environmental Protection Agency (EPA)

*Emergency Planning and Community Right-To-Know Act*

*Toxics Release Inventory*: Listed substance subject to reporting requirements.

## References

- Bucheli-Witschel M, Egli T. 2001. Environmental fate and microbial degradation of aminopolycarboxylic acids. *FEMS Microbiol Rev* 25(1): 69-106.
- ChemIDplus. 2009. *ChemIDplus Advanced*. National Library of Medicine. <http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp> and select Registry Number and search on CAS number. Last accessed: 2/19/09.
- ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on nitrilotriacetic acid. Last accessed: 2/24/09.
- EPA. 2004. *Non-confidential IUR Production Volume Information*. U.S. Environmental Protection Agency. <http://www.epa.gov/oppt/iur/tools/data/2002-vol.html> and search on CAS number. Last accessed: 4/21/05.
- Evangelou MWH, Ebel M, Schaeffer A. 2007. Chelate assisted phytoextraction of heavy metals from soil. Effect, mechanism, toxicity, and fate of chelating agents. *Chemosphere* 68(6): 989-1003.
- Goyer RA, Falk HL, Hogan M. 1981. Renal tumors in rats given trisodium nitrilotriacetic acid in drinking water for 2 years. *J Natl Cancer Inst* 66(5): 869-880.
- HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB> and search on CAS number. Last accessed: 2/24/09.
- IARC. 1990. Nitrilotriacetic acid and its salts. In *Some Flame Retardants and Textile Chemicals and Exposures in the Textile Manufacturing Industry*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 48. Lyon, France: International Agency for Research on Cancer. pp. 181-212.
- IARC. 1999. Nitrilotriacetic acid and its salts. In *Some Chemicals That Cause Tumors of the Kidney or Urinary Bladder in Rodents and Some Other Substances*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 73. Lyon, France: International Agency for Research on Cancer. pp. 385-399.
- NCI. 1977. *Bioassays of Nitrilotriacetic Acid (NTA) and Nitrilotriacetic acid, Trisodium Salt, Monohydrate (Na<sub>3</sub>NTA·H<sub>2</sub>O) for Possible Carcinogenicity (CAS No. 139-13-9 [NTA], CAS No. 18662-53-8 [Na<sub>3</sub>NTA·H<sub>2</sub>O])*. Technical Report Series No. 6, DHEW Pub. No. (NIH) 77-806. Bethesda, MD: National Cancer Institute. 185 pp.
- NIOSH. 1976. *National Occupational Hazard Survey (1972-74)*. DHEW (NIOSH) Publication No. 78-114. Cincinnati, OH: National Institute for Occupational Safety and Health.
- NIOSH. 1990. *National Occupational Exposure Survey (1981-83)*. National Institute for Occupational Safety and Health. Last updated 7/1/90. <http://www.cdc.gov/noes/noes1/80058sic.html>, <http://www.cdc.gov/noes/noes1/m0951sic.html>, <http://www.cdc.gov/noes/noes1/x9062sic.html>.
- Rakshit A. 2002. Gas chromatographic and mass spectrometric analysis of nitrilotriacetic acid in environmental aqueous samples. *J AOAC Int* 85(1): 50-55.
- Schmidt CK, Fleig M, Sacher F, Brauch HJ. 2004. Occurrence of aminopolycarboxylates in the aquatic environment of Germany. *Environ Pollut* 131(1): 107-124.
- SRI. 2009. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 6/2/09.
- TRI. 2009. *TRI Explorer Chemical Report*. U.S. Environmental Protection Agency. <http://www.epa.gov/triexplorer> and select Nitrilotriacetic Acid. Last accessed: 6/2/09.