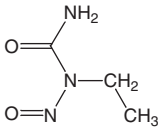
N-Nitroso-*N*-Ethylurea
CAS No. 759-73-9

Reasonably anticipated to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)



Carcinogenicity

N-Nitroso-*N*-ethylurea is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1972, 1978, 1987). When administered orally, the chemical induced malignant neurogenic tumors in the brain, spinal cord, and peripheral nervous system in rats, and neoplasms of the eye, liver, brain, kidney, muscle, and jaw of opossums. When administered in the drinking water, *N*-nitroso-*N*-ethylurea induced stomach papillomas, sarcomas, and sarcomas of the large intestine in male rats and adenocarcinomas of the mammary gland and leukemias in rats of both sexes.

When administered by subcutaneous injection, *N*-nitroso-*N*-ethylurea induced hepatomas, hepatocellular carcinomas, lung adenomas, and adenocarcinomas, lymphomas, and tumors of the peripheral nervous system, spinal cord, and brain in rats. When administered by intraperitoneal injection, the compound induced intracranial neurogenic and renal epithelial neoplasms and malignant tumors of the liver, kidney, ovary, lung, harderian gland, stomach, and lymphoreticular system in mice, and thymic lymphomas and myeloid leukemia in rats. When administered intravenously, *N*-nitroso-*N*-ethylurea induced leukemia, gliomas of the brain, and malignant tumors of the uterus and vagina in rats, and malignant tumors of the ovary, uterus, vascular endothelium, bone, bone marrow, and skin in monkeys. Prenatal exposure by intraperitoneal injection of *N*-nitroso-*N*-ethylurea induced pulmonary adenomas, tumors of endocrine glands, and tumors of the central and peripheral nervous systems in the offspring of mice. Prenatal exposure by intravenous injection of the compound induced malignant neurogenic tumors and neuroectodermal tumors in the offspring of rats, tumors of the nervous system in the offspring of hamsters, kidney adenomas, adenocarcinomas, and adenocarcinosarcomas in the offspring of rabbits, adenomas of the sweat glands and papillomas of the skin in the offspring of pigs. Prenatal exposure by oral administration of *N*-nitroso-*N*-ethylurea induced tumors of the brain, spinal cord, and trigeminal nerve in the offspring of rats (IARC 1978).

No adequate human studies of the relationship between exposure to *N*-nitroso-*N*-ethylurea and human cancer have been reported (IARC 1978).

Properties

N-Nitroso-*N*-ethylurea is a yellow to pink crystalline solid. It is soluble in water and in polar organic solvents and insoluble in nonpolar organic solvents. This compound is highly reactive, is sensitive to humidity and light, and should be stored at temperatures below -10°C. Its stability in aqueous solutions is pH dependent (pH 4.0, half-life 190 hours; pH 6.0, half-life 31 hours; pH 7.0, half-life 1.5 hours; pH 8.0, half-life 0.1 hours; pH 9.0, half-life 0.05 hours, at 20°C) (IARC 1972, 1978). In alkaline solutions, it decomposes to diazoethane. When heated to decomposition, it emits toxic fumes of nitrogen oxides (HSDB 2001).

Use

N-Nitroso-*N*-ethylurea has been used to synthesize diazoethane in the laboratory. Its mutagenic effect has been studied for promoting the growth of various plants (IARC 1978).

Production

N-Nitroso-*N*-ethylurea was first prepared in 1919, but has never been produced in commercial quantities in the United States. It is available in small quantities for laboratory research. The 1979 TSCA Inventory identified one domestic company that produced approximately 500 lb of this chemical in 1977 (TSCA 1979). No other production data were located. Chem Sources (2001) identified eight U.S. suppliers of this chemical.

Exposure

The potential for human exposure is limited because *N*-nitroso-*N*-ethylurea is not produced or used in large quantities in the United States According to the Toxic Chemicals Release Inventory (TRI), a total of 169 lb were released to the environment from two industrial facilities in 1999. About 95% of the total was released from one facility. No environmental releases were reported in prior years (TRI99 2001).

Occupational exposure may occur through inhalation or dermal contact at facilities where this chemical is used in research. In air, it exists solely as vapor where it is degraded (estimated half-life of 3.2 days) by reaction with photochemically-produced hydroxyl radicals. It hydrolyzes in water (half-life 1.5 hours at pH 7 at 20°C) (HSDB 2001). Data on the numbers of workers potentially exposed were not located.

Regulations

EPA

Clean Water Act
- Effluent Guidelines: Listed as a Toxic Pollutant (nitrosamines)
- Water Quality Criteria: Based on fish/shellfish and water consumption = 0.0008 µg/L (nitrosamines); based on fish/shellfish consumption only = 1.24 µg/L (nitrosamines)

Comprehensive Environmental Response, Compensation, and Liability Act
- Reportable Quantity (RQ) = 1 lb

Emergency Planning and Community Right-To-Know Act
- Toxics Release Inventory: Listed substance subject to reporting requirements

Resource Conservation and Recovery Act
- Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U176
- Listed as a Hazardous Constituent of Waste

FDA

Action level for *N*-nitrosamines in rubber baby bottle nipples is 10 ppb

REFERENCES

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