# AMITROLE CAS No. 61-82-5 First Listed in the Second Annual Report on Carcinogens



## CARCINOGENICITY

Amitrole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1974, 1982, 1986, 1987, 2001). When administered in the diet, amitrole increased the incidence of hepatocellular carcinomas and adenomas in mice of both sexes. When administered to weanling mice of both sexes by gavage and followed by dietary administration, amitrole induced tumors of the thyroid and increased the incidence of tumors of the liver. When mice of both sexes were nursed by dams fed diets containing amitrole, the incidence of hepatocellular carcinomas and adenomas was increased in males, but not females. When administered topically, amitrole did not induce skin tumors in mice of both sexes. One study of transplacental exposure to amitrole by mice yielded inconclusive results. When administered in the diet, amitrole induced malignant and benign tumors of the thyroid in rats of both sexes, and benign pituitary tumors in female rats. When administered in the diet, no carcinogenic effect was observed in hamsters of both sexes (IARC 1974, 1986, 2001).

No adequate data were available to evaluate the carcinogenicity of amitrole in humans. In a small cohort study of Swedish railroad workers who had sprayed herbicides, there was a statistically significant excess of all cancers among those exposed to both amitrole and chlorophenoxy herbicides, but not among those exposed mainly to amitrole (IARC 1974, 1986, 2001).

## PROPERTIES

Amitrole occurs as colorless to white crystals or as a crystalline powder. It is odorless and has a bitter taste. It is readily soluble in water, methanol, ethanol, and chloroform, and insoluble in hydrocarbons, acetone, and ether. Amitrole forms salts with most acids or bases and is a powerful chelating agent. It is corrosive to aluminum, iron, and copper (IPCS 1994, HSDB 2001). The technical grade amitrole contains a minimum of 95% active ingredient and is formulated as a solution of 250 g/L in water, typically with an equimolar concentration of ammonium thiocyanate, or as a 400 g/kg wettable powder, generally in combination with other herbicides (IPCS 1994).

### USE

Amitrole was first patented for use in the United States in 1954 (NCI 1985). Amitrole is primarily used as a post-emergent non-selective herbicide and has a wide spectrum of activity against annual and perennial broad leaf and grass type weeds. Approved uses of amitrole on soil are either for non-crop land prior to sowing, or for inter-row weed control in tree and vine crops, where contact to food plants is avoided. It is also used for the control of pondweeds (IPCS 1994).

**Amitrole (Continued)** 

#### PRODUCTION

Amitrole is currently manufactured or formulated in several countries; although its use in the U.S. has declined, amitrole remains a widely used herbicide (IPCS 1994). Chem Sources (2001) identified 15 U.S. suppliers of amitrole. It was not reported to be produced commercially in the U.S. in 1982; however, imports that year were reported to be 456,000 lb, which is a low value compared to the 1.2 million lb imported into the U.S. in 1978 (HSDB 2001).

#### **EXPOSURE**

The primary routes of potential human exposure to amitrole are inhalation and dermal contact. For the general population, exposure may occur mainly through ingestion of contaminated food or drinking water or inhalation of contaminated air near areas of high usage, such as herbicidal spraying (HSDB 2001). No residues of amitrole, however, have been detected in food and water following recommended use (IPCS 1994).

Particulates containing amitrole may be released during its production. Atmospheric levels ranging up to 100 mg/m<sup>3</sup> and river concentrations from 0.5 to 2 mg/L have been measured near one industrial facility (IPCS 1994). After application, amitrole can persist in soil for several weeks and in water for more than 200 days. The potential for exposure to amitrole exists during its manufacture or packaging and during its application as an herbicide. According to the National Institute for Occupational Safety and Health (NIOSH), approximately 83 workers were possibly exposed to amitrole in 1984, but no data were available on the number of people who potentially are exposed during its application or on the possible exposure levels in the public (HSDB 2001).

EPA's Toxic Chemical Release Inventory (TRI) lists 1999 emissions of amitrole at three facilities in the U.S. Two of the three facilities reported a total release of 7 lb to air; one plant reported a 1 lb surface water discharge. Two plants reported a total offsite release of 168 lb (TRI99 2001).

#### REGULATIONS

EPA regulates amitrole under the Comprehensive Environmental Response Compensation, and Liability Act (CERCLA), Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), and Resource Conservation and Recovery Act (RCRA). Under RCRA and CERCLA, EPA subjects amitrole to reporting requirements. Amitrole is registered under FIFRA for use as a herbicide along railroad and highway rights-of-way and on industrial tracts. There are no tolerances or tolerance exemptions. A reportable quantity (RQ) of 10 lb has been established for the compound.

ACGIH recommends a threshold limit value (TLV) of 0.2 mg/m<sup>3</sup>. NIOSH also recommends a TWA of 0.2 mg/m<sup>3</sup> for amitrole. OSHA regulates amitrole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 13.

## REFERENCES

Chem Sources. Chem Sources International, Inc. http://www.chemsources.com, 2001.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. 2-Amino-1,3,4-Triazole. Profile last updated August 9, 2001. Last review date February 6, 1991.

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IPCS. International Programme on Chemical Safety. WHO Environmental Health Criteria No. 158 Amitrole. <u>http://www.inchem.org/documents/ehc/ehc158.htm</u>, 1994.

NCI. National Cancer Institute, Division of Cancer Etiology. Monograph on the Potential Carcinogenic Risk to Humans: Amitrole. Technical Report No. 84-737. Bethesda, MD: Department of Health and Human Services, 1985.

TRI99. Toxic Chemical Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). Available from the U.S. Environmental Protection Agency Office of Environmental Information, <u>http://www.epa.gov/triexplorer/reports.htm</u>, 2001.