o-NITROANISOLE CAS No. 91-23-6

First Listed in the *Eighth Report on Carcinogens*

$$O_2N$$

CARCINOGENICITY

o-Nitroanisole is reasonably anticipated to be a human carcinogen based on sufficient evidence of malignant tumor formation at multiple tissue sites in multiple species of experimental animals (NTP 1993).

When administered in the diet to male and female rats, *o*-nitroanisole induced increased incidences of mononuclear cell leukemia and neoplasms of the urinary bladder, kidney, and large intestine. When administered in the diet to mice, *o*-nitroanisole induced increased incidences of benign and malignant hepatocellular neoplasms in males and increased incidences of hepatocellular adenomas in females.

No adequate human studies of the relationship between exposure to *o*-nitroanisole and human cancer have been reported (IARC 1996).

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

o-Nitroanisole is genotoxic in a wide variety of bacteria and mammalian cellular assays, and mutagenic and carcinogenic metabolites have been described (NTP 1993, IARC 1996).

No data were available that would suggest that the mechanisms thought to account for tumor induction by *o*-nitroanisole in experimental animals would not also operate in humans.

PROPERTIES

o-Nitroanisole is a colorless to slightly yellow liquid with a boiling point of 277°C and a melting point of 9.4°C. It is insoluble in water but is soluble in most organic solvents, including alcohol and ether. o-Nitroanisole is stable under normal laboratory conditions (NTP 2001, HSDB 2001).

USE

o-Nitroanisole is used primarily as a precursor to o-anisidine, which is prepared by direct nitro-reduction. o-Anisidine is used extensively in the synthesis of azo dyes either directly after being converted to a diazonium salt or as a precursor for the preparation of dianisidine, which is diazotized and coupled. Directly or indirectly, o-anisidine is used in the manufacture of over 100 azo dyes (NTP 1993). o-Nitroanisole has also been used as an intermediate for pharmaceutical preparation (IARC 1996).

PRODUCTION

o-Nitroanisole is produced by treating 2-chloronitrobenzene with sodium methoxide under heat and pressure. The product separates as an oil after dilution with water (IARC 1996). Of the 5 U.S. plants reporting production or import use of o-nitroanisole in the 1977 TSCA Inventory, the one known manufacturer reported a production volume of 100,000 to 1,000,000 lb/year (TSCAPP 1983), the three known importers did not report volume information, and one plant's role was unknown. In 1976 and 1978, imports of the compound through principal U.S. customs districts were reported to total 702,643 and 541,850 lb, respectively (HSDB 2001). No current data on imports or exports of o-nitroanisole are available. Chem Sources (2001) identified 10 U.S. suppliers of o-nitroanisole.

EXPOSURE

The primary routes of potential human exposure to *o*-nitroanisole are dermal contact, ingestion, and inhalation. Human exposure might be associated with its widespread use in the manufacture of azo dyes (NTP 1993). *o*-Nitroanisole was not included in the National Occupational Hazard Survey or the National Occupational Exposure Survey conducted by NIOSH (1990). *o*-Nitroanisole may be released into the environment through various waste streams by dyes and pharmaceutical manufacturing facilities. *o*-Nitroanisole has been found in drinking water. Neither volatilization nor biodegradation are expected to be important processes. When released into water, *o*-nitroanisole may adsorb to sediments and suspended solids. Volatilization is very slow, as the half-life from a model river was approximately 105 days and from a model pond was approximately 772 days. *o*-Nitroanisole will not bioaccumulate in aquatic organisms and has moderate mobility when released to soil. *o*-Nitroanisole will remain in vapor phase in the ambient atmosphere. It is degraded in the atmosphere by reactions with photochemically produced hydroxyl radicals, with an estimated half-life of 109 hr (HSDB 2001).

REGULATIONS

Atmospheric emissions of *o*-nitroanisole are regulated by the EPA under the Clean Air Act (CAA).

OSHA regulates *o*-nitroanisole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 120.

REFERENCES

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

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. *o*-Nitroanisole. Profile last updated May 15, 2001. Last review date, May 16, 1996.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Printing Processes and Printing Inks, Carbon Black and Some Nitro Compounds. Vol. 65. 578 pp. Lyon, France: IARC, 1996.

NIOSH. National Institute for Occupational Safety and Health. National Occupational Exposure Survey (1981-83). Unpublished provisional data as of 7/1/90. Cincinnati, OH: Department of Health and Human Services, 1990.

NTP. National Toxicology Program. NTP Chemical Repository. *o*-Nitroanisole. Last updated August 13, 2001.

NTP. National Toxicology Program. Technical Report Series No. 416. Toxicology and Carcinogenesis Studies of *o*-Nitroanisole (CAS No. 91-23-6) in F344 Rats and B6C3F₁ Mice (Feed Studies). NIH Publication No. 93-3147. 473 pp. National Toxicology Program, Research Triangle Park, NC, and Bethesda, MD, 1993.

TSCAPP. Toxic Substances Control Act Plant and Producers. Database available on the Chemical Information System, Version 5.0/2.0, September 1983.