

## Amphetamine and Its Salts

Amphetamine is a central nervous system (CNS) stimulant that exerts its effects by modulating several key neurotransmitters in the brain, including dopamine, serotonin, and norepinephrine. It is used as an appetite suppressant and as a drug for treating attention deficit disorder / attention deficit hyperactivity disorder in adults and children, and narcolepsy in adults. Amphetamine is also used illegally as a performance enhancer and as a CNS stimulant. Amphetamine has been detected in surface and urban waste waters. The form in which amphetamine is taken may include one or both of its enantiomers (dextro-amphetamine and levo-amphetamine). It may also be taken as an amphetamine salt, such as the hydrochloride or the sulfate salt. Exposure occurs through intentional consumption of the drug. It is unclear the extent to which the general population may be exposed as a result of the presence of amphetamine in some surface and urban waste waters or in structures formerly containing illegal drug laboratories.

Amphetamine and its salts passed the human data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

### Epidemiological data

- Case-control studies
  - Study of Hodgkin's Disease: Newell *et al.* (1973)
  - Study of Malignant Lymphoma (Hodgkin's Disease): Boston Collaborative Drug Surveillance Program (1974)
  - Healthcare plan-based study of non-Hodgkin's lymphoma, multiple myeloma, and leukemia: Doody *et al.* (1996)
  - Population-based study of non-Hodgkin's lymphoma: Nelson *et al.* (1997)
  - Multiple population-based studies of kidney cancer or renal cell carcinoma: Yu *et al.* (1986); McCredie and Stewart (1992); Lindblad *et al.* (1994); Mellemgaard *et al.* (1995); Yuan *et al.* (1998)
  - Study of ovarian cancer: Harlow *et al.* (1998)
  - Population-based study of breast cancer in men: Thomas *et al.* (1992)
- Case-control study in children
  - Study of childhood acute lymphoblastic leukemia in children <14 years of age: Wen *et al.* (2002)

### Animal carcinogenicity data

- Two-year feeding studies
  - Studies of dl-amphetamine sulfate in male and female B6C3F<sub>1</sub> mice: NTP (1991)
  - Studies of dl-amphetamine sulfate in male and female F344/N rats: NTP (1991)

- Tumor promotion/metastases studies
  - Mammary tumor promotion study in female C3H/He mice carrying the mammary tumor virus: Freire-Garabal *et al.* (1992)
  - Tumor promotion study in female Balb/c mice infected with Moloney sarcoma virus: Freire-Garabal *et al.* (1998)
  - Tumor metastases study of Walker-256 carcinoma in male Sprage-Dawley rats: Freire-Garabal *et al.* (1996)

### Other relevant data

- Genotoxicity
  - *In vitro* DNA-cell-binding assay: Kubinski *et al.* (1981)
  - *In vivo* mouse bone marrow micronucleus assay: Tariq *et al.* (1987)
  - *In vivo* DNA damage assays in rat hippocampus: Andreazza *et al.* (2008)
  - Dominant lethal assay in rats: Larez *et al.* (1979)
- Immune suppression: reviewed in Freire-Garabal *et al.* (1996)

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<sup>1</sup> Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.

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