N-Nitrosohexamethyleneimine

N-Nitrosohexamethyleneimine is a cyclic nitrosamine. It is used as an explosive in ejector seats in military jet fighter planes. Exposures to N-nitrosohexamethyleneimine may occur as a result of the manufacture and use of the chemical. N-Nitrosohexa-methyleneimine can be formed in the body in the presence of nitrosating agents from chemicals containing the hexamethyleneimine moiety, such as the hypoglycemic drug tolazamide.

N-nitrosohexamethyleneimine passed the animal 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

No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Drinking water studies in rats
  - Male Sprague-Dawley rats (administered treated drinking water five days per week for 30 or 50 weeks, and then observed for life; all rats died by 40 weeks): Lijinsky and Taylor (1979)
  - Female F344 rats (administered treated drinking water five days per week for 28 weeks and then observed for life; all rats died by 38 weeks): Lijinsky and Reuber (1981)
  - Male and female MRC (Wistar) rats (administered treated drinking water five days per week for eight or 60 weeks, and then observed for life): Goodall *et al*. (1968)

- Drinking water studies in mice
  - Male and female NZB, NZC, NZO and NZY mice (administered treated drinking water five days per week for eight weeks, and then observed for life): Goodall and Lijinsky (1984)

- Oral gavage studies in mice
  - Female BALB/c, SENCAR and CD-1 mice (twice per week for 30 weeks, and then observed for life): Strickland *et al*. (1988)

- Subcutaneous injection studies
  - Male and female Syrian golden hamsters (once per week for life): Althoff *et al*. (1973)
  - Male and female Syrian golden hamsters (one injection, and then observed for life): Althoff *et al*. (1972)

- Male and female Swiss mice (one injection, and then observed for life): Althoff *et al*. (1972)

Other relevant data

- Genotoxicity
  - *In vivo* DNA binding in rat liver: Ross and Lawson (1982)

- Structure activity considerations
  - Structurally similar to three other cyclic nitrosamines that are Proposition 65 carcinogens: N-Nitrosopiperidine, N-Nitrosopyrrolidine, and N-Nitrosomorpholine.
  - Structurally similar to 2,6-dimethyl-n-nitrosomorpholine,[1] another cyclic nitrosoamine with positive evidence of carcinogenicity.

References[2]

Althoff J, Pour P, Cardesa A, Mohr U (1972). Comparative studies of neoplastic response to a single dose of nitroso compounds. 1. The effect of N-nitrosohexamethyleneimine in Syrian golden hamsters and Swiss mice. *Z Krebsforsch Klin Onkol Cancer Res Clin Oncol* **78**(1):78-81.

Althoff J; Cardesa A; Pour P; Mohr U (1973). Carcinogenic effect of N-nitroso-hexamethylenimine in Syrian golden hamsters. *J Natl Cancer Inst* **50**(2):323-9.

Goodall CM, Lijinsky W, Tomatis L (1968). Tumorigenicity of N-nitrosohexa-methyleneimine. *Cancer Res* **28**(7):1217-22.

Goodall CM and Lijinsky W (1984). Strain and sex differences in N-nitrosohexa-methyleneimine carcinogenesis in NZB, NZC, NZO, and NZY mice. *J Natl Cancer Inst* **73**(5):1215-8.

Strickland PT, Lijinsky W, Thomas B, Kovatch RM (1988). Strain comparison of systemic N-nitrosohexamethyleneimine carcinogenesis in BALB/c, SENCAR and CD-1 mice. *Cancer Lett* **41**(2):139-46.

Lijinsky W, Taylor HW (1979). Carcinogenicity of methylated derivatives of N-nitrosodiethylamine and related compounds in SD rats. *J Natl Cancer Inst* **62**(2):407-10.

Lijinsky W, Reuber MD (1981). Carcinogenic effect of nitrosopyrrolidine, nitrosopiperidine and nitrosohexamethyleneimine in Fischer rats. *Cancer Lett* **12**:99-103.

[1] See material prepared for this chemical, also in this CIC consultation package

[2] 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.

Ross AE, Lawson TA (1982). In vivo binding of N-nitrosopyrrolidine and N-nitrosohexamethyleneimine to non-purine sites on rat liver DNA. *Cancer Lett* **15**:329-34.