

BIS(CHLOROMETHYL)ETHER AND CHLOROMETHYL METHYL ETHER (TECHNICAL-GRADE) (Group 1)

A. Evidence for carcinogenicity to humans (*sufficient*)

Numerous epidemiological studies¹⁻⁹ and case reports¹⁰⁻¹³ from around the world have demonstrated that workers exposed to chloromethyl methyl ether and/or bis(chloromethyl)-ether have an increased risk for lung cancer. Among heavily exposed workers, the relative risks are ten fold or more. Risks increase with duration and cumulative exposure. Histological evaluation indicates that exposure results primarily in lung cancer of the small-cell type⁸. Maximal relative risks appear to occur 15-20 years after first exposure⁶, and latency is shortened among workers with heavier exposure^{5,11}.

B. Evidence for carcinogenicity to animals (*sufficient*)

Bis(chloromethyl)ether produced tumours at the site of its administration to mice after exposure by inhalation^{1,14}, skin application¹ or subcutaneous injection^{1,15} and was an initiator of mouse skin tumours¹⁵; it also increased the incidence of lung tumours after its subcutaneous administration¹. In rats, it produced tumours of the respiratory tract (lung tumours and nasal-cavity carcinoma) after exposure by inhalation^{14,16-18}.

Technical-grade chloromethyl methyl ether produced local sarcomas in mice after its subcutaneous administration and was an initiator of mouse skin tumours¹; in rats and hamsters, it produced a low incidence of tumours of the respiratory tract after exposure by inhalation¹⁹.

C. Other relevant data

A slight increase in the incidence of chromosomal aberrations was observed in peripheral lymphocytes of workers exposed to bis(chloromethyl)ether or chloromethyl methyl ether in the preparation of ion-exchange resins²⁰.

Bis(chloromethyl)ether did not cause chromosomal aberrations in bone-marrow cells of rats treated *in vivo*. It induced unscheduled DNA synthesis in human fibroblasts *in vitro* and was mutagenic to bacteria²⁰.

Chloromethyl methyl ether enhanced virus-induced transformation of Syrian hamster embryo cells and was mutagenic to bacteria²⁰.

References

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