

Methyl Chloride (Chloromethane)

Methyl chloride, also known as chloromethane, is used in the manufacture of silicone rubber, and was previously used as a refrigerant and anesthetic. The chemical is formed during the chlorination of drinking water and is present in cigarette smoke. It is also the most common halogenated hydrocarbon present in the atmosphere. Methyl chloride is formed in the oceans through natural processes (e.g., a photochemical reaction between marine phytoplankton and chloride) and from biomass burning.

Methyl chloride passed the human and animal data screens, 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
 - Hospital-based study of occupationally exposed women with non-Hodgkin lymphoma: Barry *et al.* (2011)
 - *Increased risk of follicular lymphoma (Odds Ratio (OR)=1.96 [Confidence Interval (CI): 1.06-3.63]) and marginal zone lymphoma (OR=2.73 [CI: 1.07-6.98])*
 - *Among women homozygous wild-type for CYP2E1 rs2070673 polymorphism, methyl chloride exposure was significantly associated with total non-Hodgkin lymphoma (OR=2.37 [CI: 1.24-4.51]) and follicular lymphoma (OR=2.73 [CI: 1.11-6.73])*
- Prospective cohort studies
 - Studies of crewmembers on a fishing vessel accidentally exposed to methyl chloride used as a refrigerant: Rafnsson and Kristbjornsdottir (2014) and Rafnsson and Gudmundsson (1997)
 - *Increased risk of kidney cancer (Hazard Ratio (HR)=9.35 [CI: 1.28–68.24]) after 40 years of follow-up: Rafnsson and Kristbjornsdottir (2014)*
 - *Non-significant increased risk of all cancers (crude Rate Ratio (RR)=2.3 [CI: 0.9-5.5]) and lung cancer (crude RR=2.9 [CI: 0.1-55.6]) after 32 years of follow-up: Rafnsson and Gudmundsson (1997)*
- Retrospective cohort studies:
 - Study of male chemical workers in a production unit of various chlorinated methanes in US: Ott *et al.* (1985)
 - *No association of chemical exposure with pancreatic cancer or all cancers, but unable to determine specific exposure to methyl chloride*
 - Study of male synthetic butyl rubber-manufacturing workers: Holmes *et al.* (1986)
 - *No association of methyl chloride exposure with all cancers or lung cancer*

- Study of male chemical workers in Louisiana with exposures to methyl chloride and multiple other chemicals: Olsen *et al.* (1989)
 - *Non-significant increase in brain and other CNS cancer and leukemia mortality compared to the US, Louisiana, or local referent populations*

Animal carcinogenicity data

- Long-term inhalation studies
 - Two-year studies in male and female B6C3F₁ mice (6 hr/day, 5 days/week): CIIT (1981), as reviewed by IPCS (2000) and US EPA (2001)
 - *Increase in renal cortical adenomas (by pairwise comparison and trend) and renal cortical adenocarcinomas (by pairwise comparison) in males*
 - *No treatment-related tumor findings in females*
 - Two-year studies in male and female Fischer 344 rats (6 hr/day, 5 days/week): CIIT (1981), as reviewed by IPCS (2000) and US EPA (2001)
 - *No treatment-related tumor findings*

Other relevant data

- Genotoxicity: as reviewed in IPCS (2000)
 - *In vivo*
 - Covalent binding to DNA in rat liver, kidney, lung, testes (*negative*)
 - Unscheduled DNA synthesis in rat hepatocytes, spermatocytes, and tracheal epithelial cells (*negative*)
 - *In vitro*
 - Mutagenicity in *Salmonella* reverse mutation assays, *E. coli* mutation assays, and human lymphoblasts (*positive*)
 - Chromosomal aberrations in mammalian cells (*positive*)
 - Sister chromatid exchange in human lymphoblasts (*positive*)
 - DNA damage in Syrian hamster embryo cells (*positive*)
 - Unscheduled DNA synthesis in rat hepatocytes and spermatocytes (*positive*)
 - Protein binding to bovine serum albumin (*positive*)
- Structure-activity considerations:
 - Structurally similar to organohalogen Proposition 65 carcinogens, including:
 - Chloroform
 - Methylene chloride
 - Methyl iodide

Reviews

- US EPA (2001)
- IARC (1999)

References

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