ortho-Toluidine C6H4(NH2)CH3 [CAS No. 95-53-4] Occupational carcinogen: Group 1

Summary of classification

The Japan Society for Occupational Health (JSOH) recommended occupational exposure limit for ortho-Toluidine (o-Toluidine) in 1991 and classified it into Group 2A carcinogens (1986). Cohort studies focusing on the carcinogenicity of o-Toluidine are increasing. The International Agency for Research on Cancer (IARC) changed the classification of o-Toluidine from Group 2A to Group 1 (2010). A significantly increased risk, especially for the bladder cancer, was almost consistently observed in epidemiological studies¹⁻³⁾, and JSOH considers evidence in humans for the carcinogenicity of o-Toluidine as sufficient. Carcinogenesis of organs such as the spleen, liver, and bladder was confirmed by experimental animal systems, especially in multi-strain of more than one species $^{4-6}$, and evidence in experimental animals for the carcinogenicity of o-Toluidine were considered as sufficient. Mechanism studies indicated that genotoxicity of o-Toluidine was associated with carcinogenesis, and the formation of DNA adduct with o-Toluidine was confirmed in experimental animals^{7,8)}. According to a comprehensive review including these findings, JSOH proposed to change the classification of o-Toluidine to Group 1 carcinogens.

Year of Proposal (revision): 2016 Year of Proposal: 1986 (Group 2A)

References

1) Stasik MJ. Carcinomas of the urinary bladder in a

4-chloro-o-toluidine cohort. International Archives of Occupational and Environmental Health 1988; 60 (1): 21–24.

- Ward E, Carpenter A, Markowitz S, et al. Excess number of bladder cancers in workers exposed to ortho-toluidine and aniline. Journal of the National Cancer Institute 1991; 83 (7): 501–506.
- Carreon T, Hein MJ, Viet SM, et al. Increased bladder cancer risk among workers exposed to o-toluidine and aniline: a reanalysis. Occupational and Environmental Medicine 2010; 67 (5): 348–350.
- National Cancer Institute (NCI). Bioassay of o-toluidine hydrochloride for possible carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series 1979; 153: 1–147.
- Hecht SS, El-Bayoumy K, Rivenson A, et al. Comparative carcinogenicity of o-toluidine hydrochloride and o-nitrosotoluene in F-344 rats. Cancer Letters 1982; 16 (1): 103–108.
- Weisburger EK, Russfield AB, Homburger F, et al. Testing of twenty-one environmental aromatic amines or derivatives for long-term toxicity or carcinogenicity. Journal of Environmental Pathology and Toxicology 1978; 2 (2): 325–356.
- Trakoli A. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Some aromatic amines, organic dyes, and related exposures. International Agency for Research on Cancer 2010; 99: 1–658.
- IARC. Chemical agents and related occupations. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 2012; 100 (F): 9–562.
- 9) Ward EM, Sabbioni G, DeBord DG, et al. Monitoring of aromatic amine exposures in workers at a chemical plant with a known bladder cancer excess. Journal of the National Cancer Institute 1996; 88 (15): 1046–1052.