ortho-TOLUIDINE (Group 2B)

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

There are numerous studies of dyestuffs workers, dating back to the classical cohort studies in 1954. Although an excess of bladder tumours has often been found in workers exposed to varying combinations of dyestuffs and dyestuff intermediates, no population of workers exposed to *ortho*-toluidine alone has been described[1]. Occasional cases of bladder tumours have been reported in workers classified as being exposed primarily to *ortho*-toluidine, but either insufficient data or insufficient follow-up time have prevented a clear association being made with the exposure. An excess of bladder tumours was noted in workers exposed to toluene, *ortho*-nitrotoluene, *ortho*-toluidine and 4,4′-methylene bis(2-methylaniline) (see p. 248) during the manufacture of new fuchsin ('new' magenta, see p. 238) and safranine T[1,2].

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

ortho-Toluidine hydrochloride was tested for carcinogenicity in mice and rats by oral administration, producing neoplasms at various sites in both species; in particular, vascular tumours were induced, including tumours of the spleen and other abdominal haemangiosarcomas[1,3]. Following subcutaneous injection in a limited study in hamsters, no treatment-related neoplasm was observed[4]. Experiments in rabbits and guinea-pigs by subcutaneous administration were inadequate for evaluation[1].

C. Other relevant data

No data were available on the genetic and related effects of *ortho*-toluidine in humans.

ortho-Toluidine did not induce micronuclei in mice treated *in vivo*; equivocal results were obtained for sister chromatid exchanges in Chinese hamsters. It induced sister chromatid exchanges, mutation and unscheduled DNA synthesis in human cells *in vitro*. It induced transformation, aneuploidy and chromosomal aberrations in cultured rodent cells; conflicting results were obtained for sister chromatid exchanges, mutation and DNA damage. *ortho*-Toluidine caused somatic mutation in *Drosophila*. Conflicting results were obtained for mutagenicity to yeast; it induced aneuploidy, but not mitotic recombination. *ortho*-Toluidine was mutagenic to bacteria when larger amounts of an exogenous metabolic system were used than in the standard assay[5].

References

[1]*IARC Monographs, 27*, 155-175, 1982

[2]Rubino, G.F., Scansetti, G., Piolatto, G. & Pira, E. (1982) The carcinogenic effect of aromatic amines: an epidemiological study of the role of *o*-toluidine and 4,4'-methylene bis(2-methylaniline) in inducing bladder cancer in man. *Environ. Res., 27*, 241-254

[3]Hecht, S.S., El-Bayoumy, K., Rivenson, A. & Fiala, E. (1982) Comparative carcinogenicity of *o*-toluidine hydrochloride and *o*-nitrosotoluene in F-344 rats. *Cancer Lett., 16*, 103-108

[4]Hecht, S.S., El-Bayoumy, K., Rivenson, A. & Fiala, E.S. (1983) Bioassay for carcinogenicity of 3,2'-dimethyl-4-nitrosobiphenyl, *o*-nitrosotoluene, nitrosobenzene and the corresponding amines in Syrian golden hamsters. *Cancer Lett., 20*, 349-354

[5]*IARC Monographs, Suppl. 6*, 523-527, 1987