1,4-DIOXANE (Group 2B)

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

In a mortality study of 165 workers who had been exposed to low concentrations of 1,4-dioxane since 1954, seven deaths had occurred by 1975, two of which were from cancer[1].

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

Administration of 1,4-dioxane in drinking-water at several dose levels to rats and male guinea-pigs produced adenomas and carcinomas of the liver in rats of each sex, hepatomas in guinea-pigs, carcinomas of the nasal cavity in male and female rats and carcinomas of the gall-bladder in guinea-pigs. No increase in the incidence of tumours was observed in rats following its inhalation. It increased the incidence of skin tumours in mice when applied after 7,12-dimethylbenz[*a*]anthracene[2]. In a mouse-lung adenoma assay, 1,4-dioxane produced a statistically significant increase in the incidence of tumours in males given an intermediate intraperitoneal dose; no such increase was noted in males given a lower or higher intraperitoneal dose or in females given three intraperitoneal doses or in either males or females given 1,4-dioxane orally[3].

C. Other relevant data

No data were available on the genetic and related effects of 1,4-dioxane in humans. It induced DNA strand breaks in rat hepatocytes *in vitro*. It did not induce sex-linked recessive lethal mutations in *Drosophila* or aneuploidy in yeast. It induced chromosomal aberrations in plants. It was not mutagenic to bacteria[4].

References

[1]Buffler, P.A., Wood, S.M., Suarez, L. & Kilian, D.J. (1978) Mortality follow-up of workers exposed to 1,4-dioxane. *J. occup. Med.*, *20*, 255-259

[2]*IARC Monographs*, *11*, 247-256, 1976

[3]Stoner, G.D., Conran, P.B., Greisiger, E.A., Stober, J., Morgan, M. & Pereira, M.A. (1986) Comparison of two routes of chemical administration on the lung adenoma response in strain A/J mice. *Toxicol. appl. Pharmacol.*, *82*, 19-31

[4]*IARC Monographs*, *Suppl. 6*, 272-274, 1987