DICHLOROMETHANE (Group 2B)

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

No excess risk of death from malignancies was observed in one proportionate mortality study of 334 persons or in two cohort studies, one of which was a 13-year cohort mortality study of 751 employees exposed to dichloromethane, of whom 252 had had at least 20 years of work exposure, and the other a cohort study of 1271 workers in a fibre production plant in which dichloromethane was used as a solvent[1]. The first cohort study was later updated through to 1984 and expanded to comprise 1013 full-time, hourly employees. No statistically significant excess was observed for such hypothesized causes of mortality as lung cancer (14 observed, 21 expected) and liver cancer (none observed, 0.8 expected) or for cancer at any other site[2]. The proportionate mortality study and the first cohort mortality study concern partially overlapping populations. The studies had limited power to detect excess risk[1].

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

Dichloromethane was tested by oral administration in mice and rats, by inhalation exposure in mice, rats and hamsters, and by intraperitoneal injection in a lung-adenoma assay in mice. Exposure by inhalation increased the incidences of benign and malignant lung and liver tumours in mice of each sex, the incidence and multiplicity of benign mammary tumours in rats of each sex and the incidence of sarcomas located in the neck of male rats[1]. In another study in rats exposed by inhalation, an increase in the total number of malignant tumours was found in rats of each sex. After its oral administration, an increased incidence of lung tumours was seen in male mice and an increased incidence of malignant mammary tumours in female rats[3]. Other studies by oral administration in mice and in male rats and a study by inhalation in male hamsters gave negative results. Inconclusive results were

obtained after oral administration to female rats and after exposure by inhalation of female hamsters. In a mouse-lung adenoma bioassay by intraperitoneal injection, negative results were obtained[1].

C. Other relevant data

No data were available on the genetic and related effects of dichloromethane in humans.

It did not induce chromosomal aberrations in bone-marrow cells of rats or micronuclei in mice treated *in vivo*. Unscheduled DNA synthesis was not induced in human cells *in vitro*. Dichloromethane induced transformation of virus-infected Fischer rat and Syrian hamster embryo cells. It induced chromosomal aberrations, but not mutation or DNA damage, in rodent cells *in vitro*; conflicting results were reported for the induction of sister chromatid exchanges in Chinese hamster cells. It induced sex-linked recessive lethal mutations in *Drosophila*. It was mutagenic to plants and induced mutation, mitotic recombination and gene conversion in *Saccharomyces cerevisiae* under conditions in which endogenous levels of cytochrome P450 were enhanced. It was mutagenic to bacteria[4].

References

[1]*IARC Monographs, 41*, 43-85, 1986

[2]Hearne, F.T., Grose, F., Pifer, J.W., Friedlander, B.R. & Raleigh, R.L. (1987) Methylene chloride mortality study: dose-response characterization and animal model comparison. *J. occup. Med., 29*, 217-228

[3]Maltoni, C., Cotti, G. & Perino, G. (1986) *Experimental research on methylene chloride carcinogenesis.* In: Maltoni, C. & Mehlman, M.A., eds, *Archives of Research on Industrial Carcinogenesis*, Vol. IV, Princeton, Princeton Scientific Publishing, pp. 1-244

[4]*IARC Monographs, Suppl. 6*, 228-230, 1987