CHLOROFORM (Group 2B)

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

Two studies of trihalomethane levels in drinking-water supplies and community-based rates of cancer mortality have been reported. Correlations were found between these levels and various site-specific cancer mortality rates, especially those for bladder cancer, but also those for cancers of the rectum/large intestine, brain and kidney and lymphoma[1,2]. In one study in which trihalomethane levels in drinking-water at place of residence were compared directly for 395 matched pairs of female teachers with regard to colorectal cancer, no association with trihalomethane exposure was observed[3]. A mortality study of anaesthesiologists who worked at the time chloroform was used provided no significant information[4].

Several investigations have attempted to assess the effects of trihalomethanes in drinking-water indirectly by comparing risks of cancers at various sites with extent of chlorination. Although excesses of some cancers have been found, it is not possible to evaluate any effect of chloroform from such studies[5-16].

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

Chloroform produced benign and malignant tumours of the liver and kidney in mice following oral gavage[17,18]. Administration in drinking-water to female mice did not increase the incidence of liver tumours[19]. Administration of chloroform to rats by gavage or in drinking-water increased the incidences of kidney[17,19] and thyroid tumours[17] and of neoplastic nodules of the liver[20]. Chloroform was tested inadequately by subcutaneous and intraperitoneal injection in mice[17]. A study by oral administration in dogs gave negative results[21]. Oral administration of chloroform did not enhance the incidences of liver and lung tumours induced in mice by intraperitoneal injection of *N*-ethyl-*N*-nitrosourea[22], but it enhanced the incidence of liver preneoplastic foci induced in rats treated by gavage with a single dose of *N*-nitrosodiethylamine[23].

C. Other relevant data

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

Chloroform did not induce micronuclei in bone-marrow cells of mice or DNA damage in liver or kidney cells of rats treated *in vivo*. It did not induce chromosomal aberrations, sister chromatid exchanges or unscheduled DNA synthesis in human lymphocytes *in vitro*. Chloroform enhanced virus-induced cell transformation of Syrian hamster embryo cells. It did not induce sister chromatid exchanges or mutation in Chinese hamster cells or DNA damage in rat hepatocytes *in vitro*. Chloroform did not induce sex-linked recessive lethal mutations in *Drosophila* or aneuploidy, mutation or somatic segregation in *Aspergillus*. Chloroform induced DNA damage but not mutation, aneuploidy, mitotic recombination or gene conversion in *Saccharomyces cerevisiae*, whereas mutation, mitotic recombination and gene conversion were induced in *S. cerevisiae* under conditions in which endogenous levels of cytochrome P450 were enhanced. Chloroform did not induce mutation or DNA damage in bacteria[24].

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