MUSTARD GAS (SULPHUR MUSTARD) (Group 1)

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

The mortality of British and American veterans who were exposed to mustard gas during the First World War has been compared with that of other veterans who experienced respiratory infections; the effect of smoking could not be directly controlled for in either group. Cumulative lung cancer risk was not affected in UK veterans and was only modestly elevated (relative risk, 1.5, compared with the effect of cigarette smoking, roughly 10) in US veterans[1].

In contrast, mustard gas production workers in Japan during the Second World War have been found to have experienced an increase in the proportion of deaths attributed to lung cancer (three fold) compared to the local population[1,2], and especially in respiratory cancer (40 fold) in comparison with the general population[1]. Although sophisticated analytical methods were not used, the prevalence of smoking appeared to be comparable in the exposed and unexposed groups, and there was increased risk with increased duration of exposure[3]. British workers engaged in mustard gas production during the Second World War have also been followed up. Among 511 individuals, 11 cases of cancer (nine of the larynx and two of the pharynx) were identified, whereas one would have been expected[4].

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

Mustard gas was tested for carcinogenicity in mice, producing lung tumours after its inhalation or intravenous injection and local sarcomas after its subcutaneous injection[1].

C. Other relevant data

Mustard gas is a bifunctional alkylating agent[5]. No data were available on its genetic and related effects in humans.

Evidence of covalent binding to cellular DNA, RNA and protein *in vivo* was obtained in mice injected intraperitoneally with ^{35}S-labelled mustard gas. It induced chromosomal aberrations and DNA damage in rodent cells *in vitro* and mutation in mouse lymphoma cells *in vitro* and in a host-mediated assay. It induced aneuploidy, heritable translocations, dominant lethal mutations and sex-linked recessive lethal mutations in *Drosophila*. It was mutagenic to fungi and induced DNA damage in bacteria[5].

References

[1]*IARC Monographs*, *9*, 181-192, 1975

[2]Shigenobu, T. (1980) Occupational cancer of the lungs — cancer of the respiratory tract among workers manufacturing poisonous gases (Jpn.). *Jpn. J. thorac. Dis.*, *18*, 880-885

[3]Nishimoto, Y., Yamakido, M., Shigenobu, T., Onari, K. & Yukutake, M. (1983) Long term observation of poison gas workers with special reference to respiratory cancers. *J. Univ. occup. environ. Health*, *5* (*Suppl.*), 89-94

[4]Manning, K.P., Skegg, D.C.G., Stell, P.M. & Doll, R. (1981) Cancer of the larynx and other occupational hazards of mustard gas workers. *Clin. Otolaryngol.*, *6*, 165-170

[5]*IARC Monographs*, *Suppl. 6*, 403-405, 1987