CHLOROPHENOLS (Group 2B)

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

Several cohort studies have concerned workers in the chemical industry with potential exposure to 2,4,5-trichlorophenol, 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (TCDD) and other chemicals. Mortality rates for all cancers combined were not elevated over those expected. A Danish cohort with potential exposure to 2,4-dichlorophenol, present as an

intermediate during the production of chlorophenoxy herbicides, had no increase in the incidence of cancers at all sites combined, but there were statistically significantly increased risks of soft-tissue sarcoma and lung cancer in some subcohorts. Two case-control studies conducted in different regions of Sweden showed a statistically significant association between soft-tissue sarcoma and exposure to chlorophenols; studies from New Zealand have not clearly confirmed the results from Sweden, although slightly but nonsignificantly elevated risks were seen for non-Hodgkin's lymphoma with respect to chlorophenol exposure[1,2]. A case-control study from Washington State, USA, briefly reported an increased risk of soft-tissue sarcoma in connection with exposure to chlorophenols, but only in persons of Scandinavian descent[3].

A case-control study in Sweden detected a significant association between nasal and nasopharyngeal cancer and exposure to chlorophenols, independent of exposure to wood dust[1].

B. Evidence for carcinogenicity to animals (*inadequate* for pentachlorophenol and 2,4,5-trichlorophenol; *sufficient* for 2,4,6-trichlorophenol)

Pentachlorophenol was tested in one experiment in two strains of mice and in one experiment in rats by oral administration at dose levels sufficiently high to cause mild toxicity; no carcinogenic effect was seen in either species. Pentachlorophenol was also tested in two strains of mice by subcutaneous injection of single doses; it produced hepatomas in males of one strain[4].

2,4,6-Trichlorophenol was tested in one experiment in two strains of mice by oral administration, and 2,4,5- and 2,4,6-trichlorophenols were tested in one experiment by subcutaneous injection in two strains of mice. 2,4,5-Trichlorophenol was also tested in one experiment for its promoting activity in female mice. All three experiments were considered to be inadequate[5]. In a further experiment, oral administration of 2,4,6-trichlorophenol to rats and mice caused increased incidences of hepatocellular carcinomas or adenomas in mice of each sex and increased incidences of lymphomas and leukaemias in male rats[6].

C. Other relevant data

No data were available on the genetic and related effects of 2,4-dichlorophenol, 2,3,4,6-tetrachlorophenol or 2,4,6-trichlorophenol in humans. In one study, the frequency of chromosomal aberrations but not of sister chromatid exchanges was increased in the lymphocytes of men exposed occupationally to pentachlorophenol; in a smaller study, no increase in chromosomal aberrations was observed. Neither chromosomal aberrations nor sister chromatid exchanges were observed in a single study of workers exposed to 2,4,5-trichlorophenol[7].

2,4-Dichlorophenol did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro* or mutation in bacteria[7].

Pentachlorophenol was mutagenic in the mouse spot test. It did not induce aneuploidy or sex-linked recessive lethal mutations in *Drosophila*. It induced mutation and gene conversion but not mitotic crossing-over in yeast. There were conflicting data for

mutagenicity in bacteria. Pentachlorophenol did not induce strand breaks in DNA from bacteriophage. It gave negative results in a host-mediated assay with mice using bacteria as indicators[7].

2,4,6-Trichlorophenol induced somatic mutations in the spot test in mice *in vivo*. It induced mutation but not gene conversion or crossing-over in yeast and was not mutagenic to bacteria[7].

Neither 2,3,4,6-tetrachlorophenol nor 2,4,5-trichlorophenol was mutagenic to bacteria[7].

References

[1]*IARC Monographs, 41*, 319-356, 1986

[2]Pearce, N.E., Sheppard, R.A., Smith, A.H. & Teague, C.A. (1987) Non-Hodgkin's lymphoma and farming: an expanded case-control study. *Int. J. Cancer, 39*, 155-161

[3]Woods, J.S., Polissar, L., Severson, R.K., Heuser, L.S. & Kulander, B.G. (1987) Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxy herbicide and chlorinated phenol exposure in western Washington. *J. natl Cancer Inst, 78*, 899-910

[4]*IARC Monographs, 20*, 303-325, 1979

[5]*IARC Monographs, 20*, 349-367, 1979

[6]National Cancer Institute (1979) *Bioassay of 2,4,6-Trichlorophenol for Possible Carcinogenicity (Tech. Rep. Ser. No. 155; DHEW Publ. No. (NIH) 79-1711)*, Washington DC, US Department of Health, Education, and Welfare

[7]*IARC Monographs, Suppl. 6*, 231-232, 445-447, 517-518, 533-537, 1987