CHLORDANE/HEPTACHLOR (Group 3)

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

These compounds were evaluated together because they are structurally similar and because technical-grade chlordane contains 3-10% heptachlor.

Domestic use of chlordane has been reported to be associated with cases of neuroblastoma and acute leukaemia. Aplastic anaemia and blood dyscrasias have also been associated with exposure to chlordane and heptachlor[1]. Follow-up of 4411 pesticide applicators from Florida, USA, some of whom applied chlordane/heptachlor for treatment of termites, showed an excess of lung cancer deaths (34) which increased to nearly three fold (standardized mortality ratio, 267) among those who had been licensed for 20 years or more. The excess occurred in all licensing categories (termite, household pests, fumigants), except lawn and garden. There was also a slight, but nonsignificant excess of acute myeloid leukaemia (3 deaths)[2]. Follow-up of a group of 16 126 male pesticide applicators in the USA showed a deficit of deaths from all cancers but small excesses of deaths from cancers of the lung, skin and bladder, which did not appear to be related to intensity of exposure or to time since first exposure to pesticides. No excess of deaths from lung cancer was seen in

termite-control workers (with particular exposure to chlordane and heptachlor) in comparison with other pesticide applicators[3]. Follow-up of 1403 men in two US factories where chlordane, and heptachlor and endrin were manufactured, respectively, also showed a deficit of deaths from all cancers and a small excess of lung cancer. The latter was not related to time since first exposure, and smoking habits were not documented[4]. In another study of four plants, including the two factories mentioned above, no significant excess in the incidence of lung cancer was observed. Slight excesses of lung cancer were noted in three of the four plants, and an excess of stomach cancer was seen, based on three deaths, in one plant[5]. A further study[6] of one plant included in these studies[4,5] has been reported, but the analyses were inappropriate and do not provide useful information.

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

Chlordane and heptachlor (containing about 20% chlordane) produced liver neoplasms in mice following their oral administration; results for rats were inconclusive[1]. Oral administration of chlordane or heptachlor enhanced the incidence of liver tumours induced in mice by oral administration of *N*-nitrosodiethylamine[7].

C. Other relevant data

No data were available on the genetic and related effects of chlordane or heptachlor in humans.

Chlordane did not induce dominant lethal mutations in mice; it induced sister chromatid exchanges in intestinal cells of fish treated *in vivo*. It was not mutagenic to cultured human fibroblasts, and studies on DNA damage in transformed human cells yielded conflicting results. It did not induce unscheduled DNA synthesis in cultured rodent hepatocytes; it was mutagenic to Chinese hamster V79 cells but not to rat liver cells. Evidence of inhibition of intercellular communication was obtained in rodent cell systems. Chlordane was mutagenic to plants and induced gene conversion in yeast. It was not mutagenic to bacteria and did not induce breakage of plasmid DNA[8].

Heptachlor did not induce dominant lethal mutations in mice. It induced unscheduled DNA synthesis in human fibroblast cultures but did not induce repair synthesis in cultured rodent cells. Heptachlor inhibited intercellular communication in rodent cell systems; it was not mutagenic to cultured rat liver cells. It did not induce sex-linked recessive lethal mutations in *Drosophila* or gene conversion in yeast. It was mutagenic to plants. It was not mutagenic to bacteria, but in one study, positive results were reported for technical-grade but not commercial-grade heptachlor. It did not produce breakage of plasmid DNA[8].

References

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