HEXACHLOROCYCLOHEXANES (Group 2B)

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

Four cases of leukaemia were reported in men exposed to γ-hexachlorocyclohexane (lindane) with or without other chemicals[1,2]. Cases of aplastic anaemia have also been associated with exposure to this compound[1]. Mean tissue levels of hexachlorocyclohexanes were reported to be elevated in two of three studies of autopsy patients; in one of these, in four liver cancer patients, the level of the β-isomer was abnormally high[3-5]. Mean serum levels of β-hexachlorocyclohexane were not appreciably higher in four cancer patients than in three controls[6]. Exposure to γ-hexachlorocyclohexane was recorded in case-control studies of soft-tissue sarcomas and of lymphomas[7,8] but was insufficiently frequent for any conclusion to be drawn. An increase in lung cancer mortality was observed in agricultural

workers who had used hexachlorocyclohexane (unspecified) and a variety of other pesticides and herbicides (standardized mortality ratio, 180 [95% confidence interval, 140-240])[9].

B. Evidence for carcinogenicity to animals (*sufficient* for technical-grade and the α isomer; *limited* for the β and γ isomers)

Technical-grade, α- and β-hexachlorocyclohexane and the γ isomer (lindane) produced liver tumours in mice when administered orally[1,10,11]; the technical grade also produced lymphoreticular neoplasms[10]. In two studies in rats, an increased incidence of liver tumours was observed with the α isomer[1,12], and in one study in rats a few thyroid tumours were observed with the γ isomer[1]; other studies in rats[11,13-15] were considered to be inadequate. Studies in hamsters[11] and dogs[16] were also inadequate. Technical-grade hexachlorocyclohexane and the γ isomer were tested inadequately by skin application in mice[1,10]. α-Hexachlorocyclohexane enhanced the incidence of liver neoplasms induced in rats by *N*-nitrosodiethylamine[12].

C. Other relevant data

In a single study, chromosomal aberrations were not found in workers involved in the production of γ-hexachlorocyclohexane (lindane)[17].

Technical-grade hexachlorocyclohexane, but not γ-hexachlorocyclohexane, induced dominant lethal mutations in mice; chromosomal aberrations were not found in bone-marrow cells of mice exposed to technical-grade or γ-hexachlorocyclohexane *in vivo*. γ-Hexachlorocyclohexane did not induce unscheduled DNA synthesis in human cells *in vitro* and did not induce micronuclei or chromosomal aberrations in cultured rodent cells; it induced DNA strand breaks but not unscheduled DNA synthesis. It inhibited intercellular communication in Chinese hamster V79 cells. It did not induce sex-linked recessive lethal mutations in *Drosophila*. α-Hexachlorocyclohexane was not mutagenic to yeast, but the γ isomer induced gene conversion. Neither γ- nor β-hexachlorocyclohexane was mutagenic to bacteria, and α- and β-hexachlorocyclohexane did not cause DNA damage in bacteria[17].

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