4-AMINOBIPHENYL (Group 1)

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

The extent of bladder cancer risk associated with exposure to 4-aminobiphenyl was first documented by a descriptive study in the mid-1950s: of 171 men exposed to 4-aminobiphenyl between 1935 and 1955, 19 developed bladder tumours[1]. This observation appears to have been sufficient to prompt discontinuation of production and to prevent widespread use of the chemical. In 1955, a surveillance programme was initiated on workers reported to have been exposed to the chemical: during the following 14 years, 541 men were kept under surveillance by clinical and laboratory examinations; 86 had positive or suspicious cytology of the urinary sediment some time during the observation period, and 43 developed histologically confirmed carcinoma of the urinary bladder[2].

The hypothesis that another potential carcinogen, 4-nitrobiphenyl, was actually associated with the increased bladder cancer risk among these workers was raised but was dismissed by careful reconsideration of the processes involved and the possible exposures of the workers under surveillance[3].

In a survey of cancer mortality among workers at a chemical plant producing a variety of chemicals, a ten-fold increase in mortality from bladder cancer was reported. All of the nine cases on which the excess was based had started work in the plant before 1949, and 4-aminobiphenyl was known to have been used from 1941 until 1952[4].

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

4-Aminobiphenyl was tested for carcinogenicity by oral administration in rabbits, dogs and mice and by subcutaneous administration in rats. Following its oral administration, it induced bladder papillomas and carcinomas in rabbits[1] and dogs[1,5], and neoplasms at various sites in mice, including dose-related increases in the incidences of angiosarcomas[6],

hepatocellular tumours[1,6] and bladder carcinomas[1,6]. Following its subcutaneous administration to rats, it induced tumours of the mammary gland and intestine[1].

C. Other relevant data

No data were available on the genetic and related effects of 4-aminobiphenyl in humans. It formed DNA adducts in the bladder epithelium of dogs and protein adducts in serum albumin of rats treated *in vivo*. It induced mutation in human fibroblasts and mutation, DNA strand breaks and unscheduled DNA synthesis in cultured rodent cells. 4-Aminobiphenyl was mutagenic to bacteria and induced prophage[7].

References

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