2-NAPHTHYLAMINE (Group 1)

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

Case reports and epidemiological studies conducted independently in the 1950s and 1960s showed that occupational exposure to 2-naphthylamine, either alone or as an impurity in other compounds, is causally associated with the occurrence of bladder cancer[1].

Two studies in the USA examined cancer incidence and mortality in a group of chemical workers exposed mainly to 2-naphthylamine. In one, a remarkable and significantly increased incidence of bladder cancer was found (13 observed, 3.3 expected), which was not explained by smoking habits[2]. Investigation of mortality failed to pinpoint this increased risk and suggested an excess of oesophageal cancer, which, however, was not considered to be associated with the occupational exposure[3]. Two reports on one occupational population at a dyestuffs plant in Italy documented a very high bladder cancer risk linked specifically to 2-naphthylamine production (6 deaths observed, 0.04 expected) and a clear exposure-response relationship of the risk to exposures in the plant[4,5]. Incidence studies from Japan dealing with exposure to both 2-naphthylamine and benzidine (see p. 123) showed apparently increased risks of cancer of the urinary tract and bladder and, possibly, an increased occurrence of second primary cancers at several sites, including the liver[6-8]. Case reports and ecological studies also documented the relationship between exposure to 2-naphthylamine, as well as to benzidine, and bladder cancer risk[9,10]. 2-Naphthylamine was most probably involved in the exposure to aryl amines reported in a UK study as producing a significantly increased bladder cancer risk, which was not accounted for by smoking habits[11].

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

2-Naphthylamine was tested for carcinogenicity by oral administration in many animal species and by the mouse-lung adenoma bioassay. Following its oral administration, it induced bladder neoplasms in hamsters[1], dogs[1,12-14] and nonhuman primates[1], and liver tumours in mice[1]. A low incidence of bladder carcinomas was observed in rats after its oral administration[15]. In a lung-adenoma bioassay in mice by intraperitoneal injection, 2-naphthylamine produced positive results[16].

C. Other relevant data

No data were available on the genetic and related effects of 2-naphthylamine in humans.

Mice and rabbits treated with 2-naphthylamine had increased incidences of sister chromatid exchanges; micronuclei were not induced in bone-marrow cells of mice treated *in vivo*. 2-Naphthylamine was mutagenic in the mouse spot test and induced DNA strand breaks in hepatocytes of treated rats. It formed DNA adducts in bladder and liver cells of dogs *in vivo*. It induced unscheduled DNA synthesis in human cells *in vitro* and chromosomal aberrations, sister chromatid exchanges, DNA strand breaks and unscheduled DNA synthesis in rodent cells *in vitro*. Equivocal results were obtained for mutation, but it caused morphological transformation in Syrian hamster embryo and virus-infected rat cells. 2-Naphthylamine induced aneuploidy in *Drosophila*, but equivocal results were found for sex-linked recessive lethal mutations. It caused aneuploidy, mutation and mitotic recombination in yeast and was mutagenic to plants and bacteria[17].

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