ACRYLONITRILE (Group 2A)

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

In the USA, 1345 male workers potentially exposed to acrylonitrile in a textile fibre plant and observed for 20 or more years had a greater than expected incidence of lung cancer (8 observed, 4.4 expected). The risk was greater among workers with more than five years' exposure (6 observed, 2.3 expected) or with jobs where exposure was likely to have been heavier (6 observed, 2.7 expected) than among workers with shorter duration of exposure (2 observed, 1.4 expected) or low levels of exposure (2 observed, 1.4 expected)[1,2]. Further follow-up of this cohort until 1981 revealed a continued excess of lung cancer (10 observed, 7.2 expected), although during the actual follow-up period (1976-1981) there was no excess (2 observed, 2.8 expected). The updating also showed, however, a significant excess of cancer of the prostate (6 observed, 1.8 expected)[3]. In a similar study at another US textile fibre plant, an excess of prostatic cancer (5 cases observed, 1.9 expected) was observed, but there was no excess of lung cancer[4]. In the UK, a study of 1111 male workers exposed to acrylonitrile during polymerization between 1950 and 1968 and followed for ten years or more revealed five stomach cancers (1.9 expected), two colon cancers (1.1 expected), two brain cancers (0.7 expected) and nine cancers of the respiratory tract (7.6 expected)[5]. Among 327 rubber workers exposed to acrylonitrile in the USA, excesses were noted for cancers of the lung (9 observed, 5.9 expected), bladder (2 observed, 0.5 expected) and of the lymphatic and haematopoietic system (4 observed, 1.8 expected). The risk for lung cancer was greatest among workers with five to 14 years' exposure and $\geq$15 years of latency (4 observed, 0.8 expected)[6]. Another study of rubber workers in the USA, however, showed no association between exposure to acrylonitrile and lung cancer[7]. In the Federal Republic of Germany, one study of 1469 workers exposed to acrylonitrile in 12 different plants showed excesses of bronchial cancer (11 observed, 5.7 expected) and of tumours of the lymphatic system (4 observed, 1.7 expected)[8].

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

Acrylonitrile was tested for carcinogenicity in rats by oral administration and by inhalation. Following its oral administration, it induced neoplasms of the brain, squamous-cell papillomas of the stomach and Zymbal-gland carcinomas; tumours of the tongue, small intestine and mammary gland were also reported[1,9,10]. Following its inhalation, neoplasms of the central nervous system, mammary gland, Zymbal gland and forestomach were observed[1,11].

C. Other relevant data

Acrylonitrile did not enhance the frequency of chromosomal aberrations in lymphocytes of exposed workers in one study[12].

In animals treated *in vivo*, acrylonitrile did not induce dominant lethal mutations, chromosomal aberrations (in bone-marrow cells or spermatogonia) or micronuclei in mice, or chromosomal aberrations in rat bone-marrow cells. It bound covalently to rat liver DNA

in vivo and induced unscheduled DNA synthesis in rat liver but not brain. It induced sister chromatid exchanges, mutation and unscheduled DNA synthesis but not chromosomal aberrations in human cells *in vitro*. Acrylonitrile induced cell transformation in several test systems and inhibited intercellular communication in Chinese hamster V79 cells. It did not induce aneuploidy but induced chromosomal aberrations, micronuclei and sister chromatid exchanges in Chinese hamster cells; in one study, it did not induce chromosomal aberrations or sister chromatid exchanges in rat cells *in vitro*. It induced mutation and DNA strand breaks in rodent cells *in vitro*. It induced somatic mutation in *Drosophila* and was weakly mutagenic in plants. It induced aneuploidy, mutation, mitotic crossing-over and gene conversion in fungi. Acrylonitrile was mutagenic to bacteria. Urine from treated mice and rats, but not bile from rats, was mutagenic to bacteria. It bound covalently to isolated DNA[12].

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