N-METHYL-*N'*-NITRO-*N*-NITROSOGUANIDINE (MNNG) (Group 2A)

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

Three cases of brain tumour (gliomas) and one of colon cancer have been reported from a genetics laboratory over a 13-year period. All the subjects were likely to have been exposed to MNNG for at least six to 15 years prior to death, but other carcinogens had been used in the laboratory[1,2].

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

MNNG has been tested for carcinogenicity in mice, rats, hamsters, rabbits and dogs, producing tumours at many sites. It has a predominantly local carcinogenic effect and is carcinogenic in single-dose experiments. Following its oral administration, papillomas and squamous-cell carcinomas of the oesophagus and forestomach, adenocarcinomas of the stomach, small intestine and large bowel, and sarcomas of the gastrointestinal tract were reported[3]. These findings have been extended in more recent studies after oral administration to rats[4-7], hamsters[8,9] and dogs[10,11]. After subcutaneous injection of mice, it produced lung and liver tumours and haemangioendotheliomas[12]; after intrarectal instillation in rats and guinea-pigs[13-15] and after intrauterine and intravaginal application to rats, it produced local tumours[16].

C. Other relevant data

MNNG is an alkylating agent[17]. No data were available to evaluate the genetic and related effects of this compound in humans.

MNNG induced DNA strand breaks in various organs of rats treated *in vivo*. It did not cause dominant lethal mutations in mice, but it gave positive results for mutation in the mouse spot test; it induced chromosomal aberrations and micronuclei in bone-marrow cells of mice and sister chromatid exchanges in bone-marrow cells of mice and Chinese hamsters treated *in vivo*. It induced chromosomal aberrations, sister chromatid exchanges, DNA strand breaks and unscheduled DNA synthesis in human and rodent cells *in vitro* and induced mutation in cultured rodent cells. It gave positive results in several assays for cell transformation. MNNG induced somatic and sex-linked recessive lethal mutations in *Drosophila*. It caused chromosomal aberrations, sister chromatid exchanges and mutation in plants and recombination and mutation in fungi. It was mutagenic to and caused DNA damage in bacteria, and gave positive results in host-mediated assays using bacteria or yeast as indicators and mice as hosts[17].

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