5. Summary of Data Reported and Evaluation

5.1 Exposure data

Exposure to neutrons normally occurs from a mixed irradiation field in which neutrons are a minor component. The exceptions are exposure of patients to neutron radiotherapy beams and exposures of aircraft passengers and crew. In high-altitude cities, neutrons can constitute as much as 25% of cosmic background radiation. A measure of the societal burden is the annual neutron collective dose per year^{-1}. Those values would be 4.6×10^5 person–Sv year^{-1} for the world population exposed at ground level, 350 person–Sv year^{-1} for nuclear workers and 7500 person–Sv year^{-1} for the passengers and crews of aircraft. The individual average lifetime effective dose of neutrons has been estimated to be 6 mSv for the world population exposed at ground level and 30 mSv for aircrews. The maximal lifetime doses of neutrons are estimated to be 68 mSv for the population of the high-altitude city of La Paz, Bolivia, 46 mSv for long-haul pilots and up to 130 mSv for the small proportion of nuclear workers exposed to neutrons.

5.2 Human carcinogenicity data

There are no epidemiological data adequate to evaluate whether neutrons are carcinogenic to humans.

5.3 Animal carcinogenicity data

Neutrons have been tested at various doses and dose rates with wide ranges of mean energy from various sources (reactors, ^{252}Cf, ^{235}U) for carcinogenicity in mice, rats, rabbits, dogs and rhesus monkeys. Fission-spectrum neutrons were used in most of these studies. Neutrons were also tested for carcinogenicity in mice exposed prenatally and in mice after male parental exposure.

In adult animals, the incidences of leukaemia and of ovarian, mammary, lung and liver tumours were increased in a dose-related manner, although the incidence often decreased at high doses. While a γ-ray component was present in the exposure in most studies, it was generally small, and the carcinogenic effects observed could clearly be attributed to the neutrons. Prenatal and parental exposure of mice resulted in increased incidences of liver tumours in the offspring.

In general, there was no apparent reduction in tumour incidence after exposure to low doses at a low dose rate, but enhancement of tumour incidence was often observed with high doses at a 1ow dose rate. In virtually all studies, neutrons were more effective in inducing tumours than were X-radiation or γ-radiation when compared on the basis of absorbed dose.

5.4 Other relevant data

Neutrons are uncharged particles that are penetrating and interact with atomic nuclei, generating densely ionizing charged particles, such as protons, α-particles and nuclear fragments, and sparsely ionizing γ-radiation. The densely ionizing particles produce a spectrum of molecular damage that overlaps with that induced by sparsely ionizing radiation, but they are more effective in causing biological damage because they release more of their energy in clusters of ionizing events, giving rise to more severe local damage.

Comparison of the effects of neutrons with those of X- and γ-radiation is based on the assumption that the effects are the same qualitatively and differ only quantitatively. The assumption is reasonable with regard to deterministic effects because they are, in general, caused by cell killing. Neutrons are more effective than X- and γ-radiation in causing both early and late deterministic effects. The effectiveness of neutrons is dependent on their kinetic energy and decreases with increasing energy up to about 15 MeV. The effects of neutrons are much less dependent on dose rate, fractionation, cell cycle stage and oxygenation than those of X-radiation and γ-radiation. The relative biological effectiveness of neutrons for the induction of deterministic effects is greater than 1 but not as high as those estimated for induction of cancer in experimental animals. For single doses of 1–5-MeV fast neutrons, the relative biological effectiveness values range from 4 to 12, except in the haematopoietic system for which the values are 2–3. The relative biological effectiveness is higher for later-responding tissues than for early-responding tissues.

For individual cells also, neutron energy is an important factor in the stochastic effectiveness of neutrons. The ability of surviving cells to proliferate and increase cell populations does not appear to depend on the quality of radiation; however, because of the greater effectiveness of neutrons per unit dose, the surviving population is smaller and a longer time is required for the proliferation rate to recover. This may be critical in maintenance of the integrity of a tissue.

Cells from patients with ataxia telangiectasia are hypersensitive to cell killing and to induction of micronuclei by fast neutrons, although the degree of hypersensitivity is less pronounced than for sparsely ionizing radiation.

The spectrum of DNA damage from neutrons includes clustered damage of substantial complexity and consequently reduced repairability. Neutrons are comparable to X- and γ-radiation in producing double-strand breaks, but neutron-induced DNA lesions in mammalian cells are less readily repaired than those produced by sparsely ionizing radiation.

Neutrons are very efficient at inducing transformation in rodent and human cellular systems. The relative biological effectiveness of neutrons has been reported to vary from 3 to 35; whether (or under what conditions) the efficiency of neoplastic transformation is greater at low dose rates remains unclear.

Chromosomal aberrations (including rings, dicentrics and acentric fragments) were induced in the circulating lymphocytes of people exposed in an accident involving release of neutrons in a nuclear plant and in the lymphocytes of patients exposed during neutron therapy. In the former study, there was also an increase in the frequency of numerical aberrations. Within the limits of the studies, the effect was found to be dose-dependent.

Gene mutations and chromosomal aberrations are induced in mammalian cells many times more efficiently by neutrons than by the same absorbed dose of X- or γ-radiation. Fission neutrons have been shown to induce germ-line mutations in mice, including visible dominant mutations, dominant lethal mutations, visible recessive mutations and specific locus mutations. When compared with sparsely ionizing radiation on the basis of absorbed dose, fission neutrons are many-fold more effective. Neutrons have been shown to induce *Hprt* mutations in splenic lymphocytes of mice. Point mutations in K-*Ras* and N-*Ras* oncogenes were found in malignant tissue from mice exposed to neutrons, but the mutations cannot be directly ascribed to the exposure. Neutrons have been shown to induce sister chromatid exchange, dicentrics and rings in mice and reciprocal translocations in rhesus monkey stem-cell spermatogonia.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of neutrons.

There is *sufficient evidence* in experimental animals for the carcinogenicity of neutrons.

Overall evaluation

Neutrons are *carcinogenic to humans (Group 1)*.

In making the overall evaluation, the Working Group took into consideration the following:

- When interacting with biological material, fission neutrons generate protons, and the higher-energy neutrons used in therapy generate protons and α-particles. α-Particle-emitting radionuclides (e.g. radon) are known to be human carcinogens. The linear energy transfer of protons overlaps with that of the lower-energy electrons produced by γ-radiation. Neutron interactions also generate γ-radiation, which is a human carcinogen.
- Gross chromosomal aberrations (including rings, dicentrics and acentric fragments) and numerical chromosomal aberrations are induced in the lymphocytes of people exposed to neutrons.
- The spectrum of DNA damage induced by neutrons is similar to that induced by X-radiation but contains relatively more of the serious (i.e. less readily repairable) types.

- Every relevant biological effect of γ- or X-radiation that has been examined has been found to be induced by neutrons.
- Neutrons are several times more effective than X- and γ-radiation in inducing neoplastic cell transformation, mutation *in vitro*, germ-cell mutation *in vivo*, chromosomal aberrations *in vivo* and *in vitro* and cancer in experimental animals.