Review Summary
NTP Executive Committee Working Group for the Report on Carcinogens (RG2)

Nominations: X- Radiation & Gamma- Radiation
Neutrons

Review Date: 7/22/2003

Application of criteria

Exposure
The RG2 agreed that there is significant exposure to X-radiation & Gamma-radiation and neutrons from a variety of natural (environmental exposure) and anthropogenic sources, including exposure for military, medical, and occupational purposes.

Carcinogenicity

Human Data:
X- & gamma radiation: There is sufficient evidence from studies in humans that demonstrates a strong association with exposure to X and gamma radiation and cancers of the thyroid, breast, lung and leukemia. These associations are found at relatively low doses (0.2Gy) and also in a dose-responsive manner. The risk for cancer appears to be related to age at exposure where childhood exposure is responsible for leukemia and thyroid cancers, while exposure during reproductive age is responsible for breast cancer. Lung cancer may be related to exposure later in life. Other studies have reported comparatively weaker but significant associations with exposure to X and gamma radiation and cancers of the salivary glands, stomach, colon, bladder, ovary, central nervous system, and skin.

Neutrons: There are no adequate epidemiological data available to evaluate the carcinogenicity of neutrons in humans. Epidemiology studies have investigated mainly atomic bomb survivors, exposure for medical reasons and occupational studies but the doses of neutrons reported are too low to allow for an evaluation of carcinogenicity

Animal Data:
X- & gamma radiation and Neutrons: All have been shown to be carcinogenic in all species tested including mouse, rat, rabbit, dog, and monkey. Degree of susceptibility for the induction of benign and malignant tumors is species-, strain-, age- and gender-dependent. Exposures in the early prenatal stages do not appear to increase cancer rates, but exposures in the later stages may do so. Low-energy neutrons, such as fission neutrons, are significantly more carcinogenic in animal studies than low-LET radiations, such as X radiation or gamma radiation.

Genotoxicity and mechanism:
X- & gamma- radiation: Probably the most thoroughly studied of all mutagenic agents. They induce a broad spectrum of genetic effects that including gene mutations, chromosomal aberrations, DNA strand breaks, and chromosomal instability. They induce genetic damage in

somatic cells and transmissible mutations in mammalian germ cells. DNA damage results from either direct interaction with the DNA molecule or indirectly by interaction of the DNA molecule with reactive products resulting from the degradation of water by ionizing radiation e.g., free electrons, hydrogen free radicals, hydroxyl radicals. Genetic damage observed as chromosome aberrations, mutations, etc. are primarily the result of errors in DNA repair but may also arise from errors in replication of damaged DNA.

Neutrons: Genetic effects of neutrons in both humans and experimental animals are qualitatively similar to X- & gamma- radiation. However, neutrons induce chromosomal aberrations, mutations and DNA damage more efficiently and the DNA lesions induced by neutron are more severe (higher proportion of complex aberrations) and repaired less efficiently.

Genetic changes are clearly among the events that occur in the process of converting normal cells to neoplastic cells. The genetic effects induced by X- & gamma- radiation and neutrons are thought to be one of the mechanisms by which such radiation causes cancer both in humans and laboratory animals.

Recommendation

X Radiation & Gamma Radiation

Motion: recommend that X- radiation & gamma- radiation be listed in the RoC as *known to be human carcinogens* based on sufficient evidence from studies in humans that demonstrates a strong association with exposure to X- and gamma- radiation and cancer in humans that is supported by clear evidence in laboratory animals and mechanistic considerations.
Vote on the motion: 8 yes votes to 0 no votes.

Neutrons

Motion 1: recommend that neutrons be listed in the RoC as *reasonably anticipated to be a human carcinogen* based on less than sufficient evidence from studies in humans and sufficient evidence from laboratory animals studies and supportive evidence from genetic toxicology studies. This motion did not receive a second and therefore did not carry.

Motion 2: recommend that neutrons be listed in the RoC as *known to be a human carcinogen* based on the fact that genetic effects induced by neutrons are qualitatively similar to X- & gamma- radiation and is considered to be one of the mechanisms by which such radiation causes cancer both in humans and laboratory animals. This is supported by sufficient evidence of cancer causation in experimental animals, the induction of chromosomal aberrations in humans, and the production of gamma radiation by interaction of neutrons with biological materials.
Vote on the motion: 8 yes votes to 0 no votes.