

Review Summary of the National Institute of Environmental Health Sciences (NIEHS/NTP)
RoC Review Committee (RG1)

Nomination: X- and gamma radiation and neutrons

Review Committee: RG1

Date: 2003 July 7

Major issues discussed

Application of criteria

Exposure: X- and gamma radiation and neutrons clearly meet the criteria for exposure. The entire population is exposed to all three from natural sources: X- and gamma radiation are emitted by naturally occurring substances in the earth's crust and neutrons are a component of cosmic radiation. Additional exposures may result from occupational, medical, or military activities.

Human studies:

X- and gamma radiation: Numerous studies clearly indicate a causal relationship between X- and gamma radiation exposure and human cancer. In 2000, an IARC working group concluded that X- and gamma radiation are *carcinogenic to humans*. Subsequent studies have provided additional support for this conclusion. While the complete range of tumor types induced by these radiations is not fully understood, there is strong evidence that they induce leukemia and cancers of the thyroid gland, breast, and lung. The type of cancer induced appears to be related to age at exposure. Exposure during childhood results primarily in leukemia and cancer of the thyroid gland while exposure later in life is more likely to result in cancer of the breast and lung.

Neutrons: Epidemiological data on the human carcinogenicity of neutrons were not available. In 2000, an IARC working group concluded that neutrons were *carcinogenic to humans*. This conclusion was based on sufficient evidence of carcinogenicity in experimental animals and data supporting mechanisms of action similar to X- and gamma radiation.

Experimental animal studies:

X- and gamma radiation: Numerous studies have demonstrated the carcinogenicity of these radiations in experimental animals including mouse, rat, rabbit, dog, and monkey. Among these species, radiation induced tumors have been reported in approximately 20 tissues/organs including those induced in humans, i.e., leukemia, thyroid gland, breast, and lung.

Neutrons: Numerous studies have demonstrated the carcinogenicity of neutrons in experimental animals including mouse, rat, rabbit, dog, and monkey. Among these species, neutron induced tumors have been reported in approximately 20 tissues/organs including those induced in humans, i.e., leukemia, thyroid gland, breast, and lung.

Genotoxicity and mechanism:

X- and gamma radiation: These radiations are the most thoroughly studied of all mutagenic agents. They have been shown to induce a broad spectrum of genetic effects that includes gene mutations, minisatellite mutations, chromosomal aberrations, ploidy changes, DNA strand breaks, and chromosomal instability. They induce genetic damage in somatic cells and transmissible mutations in mammalian germ cells. DNA damage results from direct interaction of ionizing

radiation with the DNA molecule or indirectly by interaction of the DNA molecule with reactive products, e.g., free electrons, hydrogen free radicals, hydroxyl radicals, resulting from the degradation of water by ionizing radiation. 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: The types of genetic damage induced by neutrons are qualitatively similar to those induced by X- and gamma radiation. However, neutrons are more efficient at inducing DNA damage and the damage is less readily repaired.

Because genetic changes are clearly among the events that occur in the process of converting normal cells to neoplastic cells, the genetic effects induced by ionizing radiation are thought to be one of the mechanisms by which such radiation causes cancer.

Other concerns: None noted.

Recommendation:

X Radiation & Gamma Radiation

RG1 recommended (7 yes/0 no) that X- and gamma radiation be listed as *known to be a human carcinogen* based on the body of evidence of cancer causation in humans and the supporting evidence in experimental animals.

Neutrons

RG1 recommended (7 yes/0 no) that neutrons be listed as *known to be a human carcinogen* based on sufficient evidence of cancer causation in experimental animals, the similarity of induced genetic damage to that caused by X- and gamma radiation, the induction of chromosomal aberrations in humans, and the production of gamma radiation by interaction of neutrons with biological materials.