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

Nomination: Nitrobenzene

Review committee: RG1

Review Date: 6/10/02

Major Issues Discussed

- Animal data

  The committee felt that the CIIT 2-year inhalation study provided sufficient evidence for carcinogenicity of nitrobenzene at multiple tissue sites in rats and mice. Male $B6C3F_1$ mice showed significant increases in alveolar/bronchiolar lung tumors and thyroid follicular cell adenomas. Female $B6C3F_1$ mice showed significant increases in mammary gland adenocarcinomas and marginal increases in hepatocellular adenomas. Male F344 and CD rats showed significant increases in hepatocellular neoplasms. Male F344 rats also showed significant increases in kidney tubular cell tumors and marginal increases in thyroid follicular cell tumors. In female F344 rats, the incidence of endometrial stromal polyps was significantly increased, and there were marginal increases in the incidence of hepatocellular neoplasms. Although the incidence of malignant tumors was relatively low, the committee felt that the presence of tumors in numerous organ sites was sufficient to establish the carcinogencity of nitrobenzene in rats and mice.

- Human data

  One case-control study reported that paternal exposure to nitrobenzene was associated with a 1.6 odds ratio of childhood brain cancer (95% CI = 0.4 to 6.1). This was the only study found in the published literature that discussed the possible relationship between human cancer and exposure to nitrobenzene. The committee agreed that the limited epidemiological data available were insufficient for direct evaluation of the potential carcinogenicity of nitrobenzene in humans.

- Human Exposure

  Approximately 3 billion pounds of nitrobenzene are produced in the United States annually and production estimates have increased more than 4-fold since 1975. Environmental and occupational exposure is likely to occur through inhalation of the vapor or dermal contact with products and water containing nitrobenzene. NIOSH estimated that 5,080 employees were potentially exposed to nitrobenzene. The committee agreed that nitrobenzene met the “significant human exposure” criteria for possible listing in the Report on Carcinogens based primarily on production estimates.

- Other Data

  Nitrobenzene is structurally related to other aromatic nitro and amino compounds that are considered by the NTP and/or IARC to be reasonably anticipated or possible human carcinogens.

  Nitrobenzene is metabolized similarly in humans and animals.

Recommendation:

Recommend nitrobenzene to be listed as *reasonably anticipated to be a human carcinogen* based on sufficient evidence in animals.

Votes 7 yes 0/no