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

Nomination: Nitromethane

Review Committee: NTP Executive Committee Working Group for the Report on Carcinogens - RG2

Meeting Date: 5/01/2002

Application of Criteria

- Exposure

  The RG2 felt that there was sufficient evidence for human exposure. Evidence of exposure is primarily occupational during the production of nitromethane and nitromethane derivatives. Consumers can be exposed to nitromethane through its use as a fuel or fuel additive in racing cars, boats and model engines, which accounts for approximately 20% of the market for this compound.

- Carcinogenicity

  The RG2 felt that the NTP two year inhalation bioassay in rats exposed to 0, 94, 188 or 375 ppm nitromethane and mice exposed to 0, 188, 375 and 750 ppm nitromethane provided sufficient evidence of carcinogenicity in experimental animals as evident by a significant increased incidence of malignant and/or a combination of malignant and benign tumors at multiple tissue sites (lung, harderian gland, liver, and mammary) in multiple species of experimental animals (rats and mice). Clear evidence of carcinogenicity was observed in male and female $B6C3F_1$ mice based on significant increased incidences of harderian gland tumors (adenoma and adenoma and carcinoma combined) and lung tumors (carcinomas in males and adenoma and carcinomas combined in females). Increased incidences in liver tumors were also observed in female mice (adenoma and adenomas and carcinomas combined). Clear evidence of carcinogenicity was also observed in female F344/N rats based on significant increase incidences of mammary gland fibroadenoma and fibroadenoma, adenoma, or carcinoma (combined). Nitromethane was not carcinogenic in Long-Evans rats treated at 100 and 200 ppm for two years.

Other Scientific Concerns

- Human Studies

  No human studies reporting on the relationship of exposure to nitromethane and human cancer were found in the literature.

- Genotoxicity and Mechanistic Concerns

  Nitromethane was not mutagenic in bacteria and does not appear to be genotoxic. Although nitromethane is structurally related to other nitro compounds (i.e. 2-nitropropane and tetranitromethane) that are reasonably anticipated to be human carcinogens, the mechanism of these compounds and nitromethane is not known. In contrast to nitromethane, these compounds are mutagenic and in general induce tumors in experimental animals at different sites than nitromethane.

Recommendation:

- Motion

  Recommend Nitromethane to be listed as *reasonably anticipated to be a human carcinogen* based on sufficient evidence in animals that indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors at multiple tissue sites in multiple species of experimental animals.

  Vote 9 yes votes to 0 no votes