

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

**Nomination:** Naphthalene

**Review committee:** RG1

**Review Date:** 6/10/02

### Major Issues Discussed

#### ◆ Animal data

The committee felt that the NTP two-year inhalation study in F344 rats provided strong evidence for the carcinogenicity of naphthalene in that species: increased incidences of respiratory epithelial adenoma and olfactory epithelial neuroblastoma of the nose were found; some of the neuroblastomas invaded the brain. The committee agreed that the evidence of carcinogenicity in B6C3F<sub>1</sub> mice was less impressive, being limited to a single sex (female), a single target site (lung), and consisting primarily of benign tumors (only one malignant tumor observed). There was some discussion as to whether the Listing Criteria of increased tumor incidence "to an unusual degree with regard to incidence, site or type" applied to the NTP naphthalene rat study, since the historical control rate of these neoplasms is essentially zero. Many felt that the observed carcinogenic response in rats was sufficient to justify listing naphthalene as *reasonably anticipated to be a human carcinogen*, regardless of the interpretation placed on the lung tumor data in female mice. Most of the committee agreed that the mechanistic data were insufficient to discount the observed carcinogenic response in rats as being irrelevant to humans.

#### ◆ Human data

The committee agreed that the very limited data available were insufficient for direct evaluation of the potential carcinogenicity of naphthalene in humans

#### ◆ Human Exposure

The primary sources of potential human exposure are environmental exposures (through inhalation of ambient and indoor air) and accidental ingestion of naphthalene-containing household products. Dermal exposure to naphthalene may also occur, through handling or wearing of clothing stored with moth repellents containing naphthalene. It was also estimated that more than 100,000 workers were exposed to naphthalene from 1981-83, and naphthalene production has been steadily increasing since that time. Thus, the Committee agreed that naphthalene met the "significant human exposure" criteria for possible listing in the Report on Carcinogens.

◆ Other Factors

The Committee noted inter-species differences in the rates of metabolism of naphthalene, nasal anatomy, and other factors. However, it concluded that none of these factors definitively established the mechanisms of naphthalene carcinogenicity or the reasons for species differences in carcinogenic response.

**Recommendation:**

The majority of the committee felt that naphthalene should be listed as *reasonably anticipated to be a human carcinogen*, based primarily on the rare nasal tumors in rats, but supported by an increased incidence of lung adenoma in female mice. There was a single dissenter, who questioned whether the nasal cavity neoplasms in rats were relevant to humans, and noted the rather limited response in mice.

Votes 6 yes 1/no