

Sapphire News

Derivation of Inhalation Toxicity Reference Values for Propylene Oxide Using Mode of Action Analysis: Example of a Threshold Carcinogen.

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Propylene oxide (PO) is an important industrial chemical used primarily in the synthesis of other compounds. Inhalation carcinogenesis studies in rodents, with NOAELs of 100 and 200 ppm, have revealed that chronic, high exposure to PO can induce tumors at the site of contact. Despite these characteristics, there is no evidence that typical environmental or occupational exposures to PO constitute a health risk for humans. The nongenotoxic effects of PO (glutathione depletion and cell proliferation) that augment its DNA-reactive and non-DNA-reactive genotoxicity are expected to be similar in humans and rodents. Available evidence on mode-of-action suggests that cancer induction by PO at the site of contact in rodents is characterized by a practical threshold. Human toxicity reference values for potential carcinogenic effects of PO were derived based on nasal tumors identified in rodent studies and specified uncertainty factors. The 95% lower confidence limit on the dose producing a 10% increase in additional tumor risk (LED10) was calculated using the rat and mouse datasets. The human reference values derived from the rat and mouse LED10 values were 0.7 and 0.5 ppm PO, respectively. A similar non-cancer reference value, 0.4 ppm, was derived on the basis of non-neoplastic nasal effects in rats.