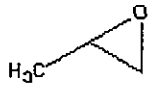
追加資料（第2回化学物質の125許価検討会 H22.4.16）

Abstract for TR-267 - Propylene Oxide (CASRN 75-56-9)

Toxicology and Carcinogenesis Studies of Propylene Oxide (CAS no. 75-56-9) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies)

Link to the full study report in PDF. If you have difficulty accessing the document, please send email to the NTP Webmaster [Send Email] and identify documents/pages for which access is required.



Chemical Formula: C_3H_6O

Propylene oxide is a volatile, colorless liquid used as an intermediate in the production of polyether polyols, polyurethane foams, and unsaturated polyester resins and also as a fumigant for sterilizing a variety of materials ranging from plastic medical instruments to foodstuffs. In the United States, propylene oxide is registered as a fumigant for packaged dried prunes and glacé fruits such as candied cherries and as an insecticidal and fungicidal fumigant for bulk quantities of cocoa, gums, and processed spices.

The 2-year carcinogenesis studies of propylene oxide (greater than 99.9% pure) were conducted by exposing groups of 50 F344/N rats and 50 B6C3F$_1$ mice of each sex to air containing propylene oxide at concentrations of 0 (chamber control), 200, or 400 ppm for 6 hours per day, 5 days per week, for 103 weeks.

The survival of rats exposed to propylene oxide was comparable with that of the controls; terminal body weights were lower than those of the controls for high dose males (8%) and high dose females (6%). Survival of exposed male and female mice decreased relative to that of the controls (male: control, 42/50; low dose, 34/50; high dose, 29/50; female: 38/50; 29/50; 10/50), but the difference was significant only for animals in the high dose groups. High dose female mice had a mean terminal body weight 22% below that of the controls.

The respiratory epithelium of the nasal turbinates was one of the primary tissues affected in male and female rats; exposure-related increases occurred in the incidences of suppurative inflammation, epithelial hyperplasia, and squamous metaplasia. Papillary adenomas, involving the respiratory epithelium and underlying submucosal glands of the nasal turbinates, were observed in three female rats and two male rats exposed to propylene oxide at 400 ppm. The incidence of adenomas in females was significant by the trend tests.

The proportions of high dose female rats with C-cell adenomas and with C-cell carcinomas of the thyroid gland were increased, but only the combined incidence of these tumors was significant (2/45; 2/35; 7/37). These tumors were not considered to be related to exposure to propylene oxide because there was no other evidence for C-cells' being a target tissue and because there was no increase in C-cell hyperplasia.

The combined incidences of female rats with endometrial stromal polyps and endometrial stromal sarcomas of the uterus were significantly increased in the dosed groups (3/49; 12/50; 10/47). However, the occurrence of these lesions in the dosed groups was similar to the average (306/1,502, 20%) seen in untreated controls in NTP carcinogenesis studies, and hence this increase was not regarded as being related to exposure to propylene oxide.

The respiratory epithelium of the nasal turbinates was also one of the primary tissues affected in

male and female mice; exposure-related increases occurred in the incidences of inflammation, and squamous metaplasia was observed in one low dose male and two high dose female mice. One squamous cell carcinoma and one papilloma occurred in the nasal cavity of different high dose male mice, and two high dose female mice had adenocarcinomas of the nasal cavity. The endothelial cells of the submucosal vascular plexus in the nasal turbinates also appeared to be a major site affected in high dose male mice. Three high dose male and three high dose female mice had a saccular dilation (classified as angiectasis) of submucosal turbinate vessels. Further, hemangiomas were seen in the nasal cavity of 5/50 high dose male mice and 3/50 high dose female mice, and hemangiosarcomas were found in the nasal cavity of 5/50 high dose male mice and 2/50 high dose female mice. The increased incidences of hemangiomas in males and females and of hemangiosarcomas in males were statistically significant. Vascular tumors were not present in the nasal turbinates of any low dose or control mice.

Under the conditions of these studies, there was some evidence of carcinogenicity for F344/N rats, as indicated by increased incidences of papillary adenomas of the nasal turbinates in male and female rats exposed to propylene oxide at 400 ppm. For male and female $B6C3F_1$ mice, there was clear evidence of carcinogenicity, as indicated by increased incidences of hemangiomas or hemangiosarcomas of the nasal turbinates at 400 ppm. In the respiratory epithelium of the nasal turbinates, propylene oxide also caused suppurative inflammation, hyperplasia, and squamous metaplasia in rats and inflammation in mice.

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Target Organs & Incidences from 2-year Studies

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