Vinyl Acetate

Vinyl acetate is a high production volume chemical used solely as an intermediate to manufacture vinyl acetate polymers and copolymers, including polyvinyl acetate, polyvinyl alcohol, polyvinyl acetals, ethylene-vinyl acetate copolymers, and polyvinyl chloride-acetate copolymers. Vinyl acetate polymers and copolymers are primarily used in adhesives for paper, wood, glass, metals and porcelain; they are also used in water-based latex paints, paper coatings, leather and textile finishings, inks, lacquers, heat sealing films, pesticides, food additives, and cosmetics. The general population may be exposed to residual vinyl acetate monomer released from products containing vinyl acetate polymers and copolymers. Occupational exposure to vinyl acetate may occur during monomer production, polymer formation, and product manufacture.

Vinyl acetate passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

- Retrospective cohort study of lung cancer risk among workers employed at a synthetic chemicals plant in the US: Waxweiler *et al.* (1981)
    - *Vinyl acetate was among 19 chemicals examined by comparing cumulative dose differences between cases and controls*
    - *No association observed between lung cancer and exposure to vinyl acetate*

- Nested case-control study nested within a cohort of workers employed at two chemical manufacturing facilities and a research and development center in the US: Ott *et al.* (1989)
    - *Vinyl acetate was among 21 chemicals examined*
    - *No association observed between any of the four types of cancer (non-Hodgkin's lymphoma, multiple myeloma, nonlymphocytic leukemia and lymphocytic leukemia) and exposure to vinyl acetate*

Animal carcinogenicity data

- Long-term inhalation studies in rats
    - 104-week studies in male and female Sprague-Dawley-derived Crl:CD(SD)BR rats (6 hours/day, 5 days/week): Bogdanffy *et al.* (1994a)
        - *Increase in rare nasal papillomas, rare nasal squamous cell carcinomas, and combined benign and malignant rare nasal tumors (by pairwise comparison and trend) in high-dose males*
        - *Increase in rare nasal squamous cell carcinoma in high-dose females*

- Long-term drinking water studies in rats
    - 100-week exposure and additional 30-week observation in male and female Fischer rats: Lijinsky and Reuber (1983)
        - *Increases in liver neoplastic nodules, uterine adenocarcinomas, and thyroid c-cell adenomas in high-dose females (each by pairwise comparison and trend)*
        - *No treatment-related tumor findings in males*
    - Lifetime studies in male and female Sprague-Dawley-derived Crl:CD(SD)BR rats (exposed pre-conception, *in utero*, lactation, and weaning through 104 weeks): Bogdanffy *et al.* (1994b)
        - *No treatment-related tumor findings*
    - Lifetime studies in male and female Sprague-Dawley rats (exposure started at 17 weeks of age and continued for 104 weeks) and their offspring (exposure started on gestation day 12, and continued through lactation and via drinking water for 104 weeks after weaning). Animals were observed until death: Minardi *et al.* (2002)
        - *Increases in rare squamous cell carcinoma of the oral cavity and lips, and rare squamous cell carcinoma of the forestomach in F0 females*
        - *Increases in rare squamous cell carcinoma of the oral cavity and rare squamous cell carcinoma of the forestomach (each by pairwise comparison and trend) in F1 males*
        - *Increases in rare squamous cell carcinoma of the oral cavity (by pairwise comparison and trend), rare squamous cell carcinoma of the tongue, and rare squamous cell carcinoma of the forestomach (by pairwise comparison and trend) in F1 females*
    - 104-week studies in male and female F344/DuCrj rats: Umeda *et al.* (2004)
        - *Increase in rare squamous cell carcinoma of the oral cavity (by pairwise comparison) in males*
        - *Increases in rare squamous cell carcinoma of the oral cavity (by trend) and c-cell carcinoma of the thyroid (by pairwise comparison) in females*

- Long-term inhalation studies in mice
    - 104-week studies in male and female Swiss-derived Crl:CD-1(ICR)BR mice (6 hours/day, 5 days/week): Bogdanffy *et al.* (1994a)
        - *No treatment-related tumor findings*

- Long-term drinking water studies in mice
    - 78-week studies in male and female Swiss mice (exposure started at 17 weeks of age) and their offspring (exposure started on gestation day 12 and continued through lactation and via drinking water for 78 weeks after weaning). Animals were observed until death: Maltoni *et al.* (1997)

        - *Increase in esophageal squamous cell carcinoma (by pairwise comparison) in F0 females*
        - *Increases in oral cavity and esophageal squamous cell carcinoma (each by pairwise comparison) in F1 males*
        - *Increases in oral cavity, tongue, esophageal, and forestomach squamous cell carcinoma (each by pairwise comparison) and Zymbal gland squamous cell carcinoma, lung adenoma, and combined lung adenoma and carcinoma (each by trend) in F1 females*
    - 104-week studies in male and female Crj:BDF_1 mice: Umeda *et al.* (2004)
        - *Increases in oral cavity squamous cell carcinoma, combined oral cavity squamous cell papilloma and carcinoma, esophageal squamous cell carcinoma, forestomach squamous cell carcinoma, and combined forestomach squamous cell papilloma and carcinoma (each by pairwise comparison) in males*
        - *Increase in oral cavity squamous cell carcinoma and combined oral cavity squamous cell papilloma and carcinoma (each by pairwise comparison) in females*

Other relevant data

- Genotoxicity as reviewed in IARC (1995) and Albertini (2013)
    - *In Vitro*
        - Mutations
            - In *Salmonella typhimurium* or *Saccharomyces cerevisiae (negative with and without exogenous activation)*
            - In L5178Y mouse lymphoma cells at the TK locus *(positive with and without exogenous activation)*
            - In human TK6 cells at the TK and HPRT loci *(positive at ≥ 250 µM)*
        - SOS repair in *E. coli* (*negative*)
        - DNA-protein cross-links in *E. coli (positive with exogenous activation)*
        - DNA cross-links
            - In rat olfactory epithelial cells *(positive without exogenous activation)*
            - In rat nasal respiratory epithelial cells *(positive without exogenous activation)*
            - In human lymphocytes *(positive without exogenous activation)*
        - Sister chromatid exchanges (SCEs)
            - In Chinese hamster ovary (CHO) cells *(positive with and without exogenous activation)*
            - In human lymphocytes *(positive without exogenous activation)*

        - Chromosomal aberrations in human lymphocytes *(positive without exogenous activation)*
    - *In Vivo*
        - Micronucleus induction
            - In mouse bone marrow *(positive)*
            - Meiotic micronucleus induction in mice *(negative)*
        - DNA adducts in liver of male and female rats *(negative)*
        - Covalent DNA binding in rat hepatocytes (^{14}C label) *(negative)*
        - SCEs in mouse cells *in vivo (positive)*
        - Abnormal sperm morphology in mice *(positive)*
- Cell transformation
    - In Syrian hamster embryo (SHE) cells *(positive without exogenous activation)*
- Mechanistic Considerations
    - Acetaldehyde, a genotoxic metabolite of vinyl acetate, is a Proposition 65 carcinogen, and is classified by IARC as "possibly carcinogenic to humans" (Group 2B).

Reviews

- IARC (1995)

References

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