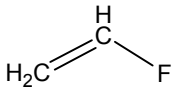
VINYL FLUORIDE
CAS No. 75-02-5
First Listed in the *Tenth Report on Carcinogens*



CARCINOGENICITY

Vinyl fluoride (VF) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. Both male and female rats exposed to VF by inhalation showed increased incidences of hepatic hemangiosarcoma, hepatocellular adenoma or carcinoma, and Zymbal gland carcinoma. Both male and female mice exposed to VF by inhalation showed increased incidences of hepatic hemangiosarcoma, bronchiolar-alveolar adenoma or adenocarcinoma, hepatocellular adenoma, and harderian gland adenoma. Female mice also showed an increased incidence of mammary gland adenocarcinoma (Bogdanffy *et al*. 1995, IARC 1995).

The tumor responses of laboratory animals to VF are similar to their responses to vinyl chloride, a known human carcinogen (IARC 1987), and to vinyl bromide, a probable human carcinogen (IARC 1986). A unique feature of vinyl chloride carcinogenicity is that vinyl chloride induces rare hepatic hemangiosarcomas in experimental animals and is causally associated with excess risk of liver hemangiosarcoma in epidemiological studies of exposed workers. The fact that VF, vinyl chloride, and vinyl bromide all induce rare hemangiosarcomas of the liver in experimental animals and induce the formation of similar DNA adducts suggests a possible common mechanism of carcinogenicity for all three of these chemicals.

No adequate human studies of the relationship between exposure to VF and human cancer were found.

OTHER INFORMATION RELATING TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

VF is mutagenic in *Salmonella typhimurium* with the addition of a rat liver homogenate metabolic activation system (DuPont de Nemours and Co. 1992). In addition, VF induces gene mutations and chromosomal aberrations in Chinese hamster ovary cells (with metabolic activation), sex-linked recessive lethal mutations in *Drosophila melanogaster*, and micronuclei in bone marrow cells of female mice (IARC 1995).

VF likely is metabolized in a manner similar to vinyl chloride: oxidation via cytochrome P450 to fluoroethylene oxide, followed by rearrangement to 2-fluoroacetaldehyde, which is oxidized to fluoroacetic acid. Human, rat, and mouse liver microsomes metabolize VF at similar rates (Cantoreggi and Keller 1997).

VF metabolites form covalent DNA adducts. Inhalation exposure of rats and mice to VF produced a dose-related increase in the formation of the promutagenic adduct N^2,3-ethenoguanine in their liver DNA (Swenberg *et al*. 1995).

No available data suggest that mechanisms by which VF induces tumors in experimental animals would not also operate in humans.

PROPERTIES

VF is a colorless gas with a faint ether-like odor. It is insoluble in water and soluble in alcohol, ether, and acetone. VF is extremely flammable and will form explosive mixtures with air. It can form hazardous polymers when heated. A fire containing VF can generate highly toxic hydrogen fluoride gas (HSDB 2001). VF reacts with alkali and alkaline earth metals, powdered aluminum, zinc, and beryllium (IARC 1995).

USE

VF is used primarily in the production of polyvinyl fluoride and other fluoropolymers. Polymers of VF are resistant to weather and have great strength, chemical inertness, and low permeability to air and water. Polyvinyl fluoride is laminated with aluminum, galvanized steel, and cellulose materials and is used as a protective surface for the exteriors of residential and commercial buildings. Polyvinyl fluoride laminated with various plastics has been used to cover walls, pipes, and electrical equipment and inside aircraft cabins (IARC 1995).

PRODUCTION

VF was first prepared in the early 1900s by reaction of zinc with 1,1-difluoro-2-bromoethane. Modern preparation of VF involves reaction of acetylene and hydrogen fluoride in the presence of a mercury-based or aluminum-based catalyst (IARC 1995). Annual U.S. production is approximately 3.3 million lb (HSDB 2001). The U.S. Environmental Protection Agency (EPA), through the Office of Pollution Prevention and Toxics, listed VF in the high production volume chemical list in 1990, indicating that annual production exceeded 1 million lb (EPA 1990). Only one U.S. manufacturer of VF was identified (HSDB 2001).

EXPOSURE

Exposure to VF in the environment will occur by inhalation, because VF released into the environment exists as a gas (IPCS 1993).

Occupational exposure to VF occurs primarily by inhalation (HSDB 2001). Skin and eye contact can occur among workers handling liquid VF. Handling liquid VF also would cause frostbite (IPCS 1993).

Occupational exposure to VF was studied in a manufacturing and polymerization facility in the United States. In eight personal air samples taken at the manufacturing facility, concentrations of VF generally were less than 2 ppm (3.76 mg/m^3). In one personal sample, however, the concentration of VF was 21 ppm (39.5 mg/m^3). VF concentrations in seven personal samples taken in the polymerization facility ranged from 1 to 4 ppm (1.88 to 7.52 mg/m^3). In four general working areas, the VF concentrations ranged from 1 to 5 ppm (1.88 to 9.4 mg/m^3) (IARC 1995).

REGULATIONS

Vinyl fluoride is regulated by EPA under the Clean Air Act to prevent accidental releases. It has a threshold reporting quantity of 1,000 lb. EPA also regulates VF under the Toxic Substances Control Act, which requires health and safety studies to determine risk of injury to human health or the environment.

NIOSH recommends for vinyl fluoride a REL (Recommended Exposure Limit) of 1 ppm as a TWA exposure up to a 10-hour workday during a 40-hour workweek and a 5 ppm ceiling.

The Occupational Safety and Health Administration regulates vinyl fluoride under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 188.

REFERENCES

Bogdanffy, M.S., G.T. Makovec, and S.R. Frame. Inhalation oncogenicity bioassay in rats and mice with vinyl fluoride. Fundam. Appl. Toxicol., Vol. 26, 1995, pp. 223-238.

Cantoreggi, S., and D.A. Keller. Pharmacokinetics and metabolism of vinyl fluoride in vivo and in vitro. Toxicol. Appl. Pharmacol., Vol. 143, 1997, pp. 130-139.

DuPont de Nemours and Co. Mutagenic activity of fluoroethylene in the Salmonella/Microsome Assay. U.S. EPA-OTS Document Id. No. 88-920002842, Washington, DC: U.S. EPA, Office of Toxic Substances, 1992.

EPA. U.S. Environmental Protection Agency. Vinyl Fluoride (CAS# 75-02-5). Office of Pollution Prevention and Toxics, http://www.epa.gov/opptintr/chemrtk/opptsrch.htm & search 75-02-5, 1990.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. Vinyl Fluoride. Profile last updated May 15, 2001. Last review date, May 11, 1995.

IARC. Some Chemicals Used in Plastics and Elastomers. Vinyl Fluoride. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 39. Lyon, France: IARC, 1986, pp. 147-154.

IARC. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans Suppl 7. Lyon, France: IARC, 1987.

IARC. Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals. Vinyl Fluoride. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 63. Lyon, France: IARC, 1995, pp. 467-475.

IPCS. International Programme on Chemical Safety & the Commission of the European Communities. Vinyl Fluoride. International Chemical Safety Cards, http://www.cdc.gov/niosh/ipcs/ipcs0598.html, 1993.

Swenberg, J.A., D.K. La, N.A. Scheller, and K.-Y. Wu. Dose-response relationships for carcinogens. Toxicol. Lett., Vol. 82/83, 1995, pp.751-756.