# Vinyl Halides (Selected)

## Introduction

Vinyl bromide, vinyl chloride, and vinyl fluoride belong to a class of structurally related chemicals referred to as "simple vinyl halides" or "halogenated olefins." These three vinyl halides are listed in the Report on Carcinogens as individual chemicals and not as a class. (The class also includes vinyl iodide, which is not listed in the Report on Carcinogens.) Vinyl chloride was first listed in the *First Annual Report on Carcinogens* (1980) as *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans, and vinyl bromide and vinyl fluoride were first listed in the *Tenth Report on Carcinogens* (2002) as *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in experimental animals.

The three listed vinyl halides have widespread industrial use, especially in the plastics industry, and the primary route of occupational exposure is inhalation. Numerous epidemiological studies of occupational exposure have shown that vinyl chloride causes cancer of the blood vessels of the liver (hepatic angiosarcoma) in humans (IARC 2008a,b,c). Hepatic angiosarcoma is a very rare type of cancer; its estimated incidence in the United States is only 25 cases per year (Molina and Hernandez 2003). In experimental animals, this type of cancer is usually referred to as hemangiosarcoma; all three listed vinyl halides cause hemangiosarcoma of the liver in experimental animals. No epidemiological studies of the carcinogenicity of vinyl bromide or vinyl fluoride have been identified. However, all three listed vinyl halides are metabolized to similar DNA-reactive intermediates (haloethylene oxide and haloacetaldehyde) via a human cytochrome P450 2E1–dependent pathway and cause genetic damage *in vivo* and *in vitro*. Furthermore, the DNA adducts formed are the same for all three of these vinyl halides, and the etheno adducts can cause DNA miscoding by modifying base-pairing sites (IARC 2008a,b,c). The fact that vinyl bromide, vinyl chloride, and vinyl fluoride all cause hemangiosarcoma of the liver in experimental animals and induce the formation of similar DNA adducts suggests a common mechanism of carcinogenicity for these three vinyl halides.

## References

IARC. 2008a. Vinyl bromide. In *1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide)*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 97. International Agency for Research on Cancer. pp. 445-457.

IARC. 2008b. Vinyl chloride. In *1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide)*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 97. Lyon, France: International Agency for Research on Cancer. pp. 311-443.

IARC. 2008c. Vinyl fluoride. In *1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide)*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 97. International Agency for Research on Cancer. pp. 459-471.

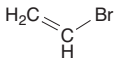
Molina E, Hernandez A. 2003. Clinical manifestations of primary hepatic angiosarcoma. *Dig Dis Sciences* 48(4): 677-682.

# Vinyl Bromide

## CAS No. 593-60-2

Reasonably anticipated to be a human carcinogen

First listed in the *Tenth Report on Carcinogens* (2002)




## Carcinogenicity

Vinyl bromide is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

### *Cancer Studies in Experimental Animals*

Exposure to vinyl bromide by inhalation caused tumors at several different tissue sites in rats. In rats of both sexes, it caused cancer of the blood vessels of the liver (hepatic hemangiosarcoma), Zymbal-gland cancer (carcinoma), and benign and malignant liver tumors (hepatocellular adenoma and carcinoma) (Benya *et al.* 1982, IARC 1986).

### *Studies on Mechanisms of Carcinogenesis*

Vinyl bromide was genotoxic in *Salmonella typhimurium* (IARC 1986) and *Drosophila melanogaster* (Ballering *et al.* 1996) and caused DNA damage in several organs of mice (Sasaki *et al.* 1998). Vinyl bromide is metabolized in a manner similar to vinyl fluoride and vinyl chloride: oxidation via cytochrome P450 to bromoethylene oxide, followed by rearrangement to 2-bromoacetaldehyde, which is oxidized to bromoacetic acid. Vinyl bromide is metabolized more slowly than vinyl chloride (by about an order of magnitude) (Bolt *et al.* 1978), which suggests that vinyl bromide's greater carcinogenic potency may be related to kinetic differences in metabolism. Vinyl bromide appears to be a more potent inducer of hepatic hemangiosarcoma in rats than is vinyl chloride.

Vinyl bromide metabolites bind covalently to DNA and to protein; 2-bromoethylene oxide is the major DNA binding agent, and 2-bromoacetaldehyde is the major protein alkylating agent (Guengerich *et al.* 1981). After exposure to vinyl chloride, the major DNA adduct formed is 7-(2-oxoethyl)guanine (constituting approximately 98% of all adducts). By analogy, the 7-position of guanine is considered to be the preferred site of DNA alkylation by bromoethylene oxide, the primary metabolite of vinyl bromide (Bolt 1988). Chloroacetaldehyde and bromoacetaldehyde can react with adenine or cytosine bases in DNA or RNA to produce cyclic etheno-DNA- and -RNA adducts (1,$N^6$-ethenoadenosine and 3,$N^4$-ethenocytosine). Etheno-DNA adducts can cause DNA miscoding by modifying base-pairing sites. Because the cyclic etheno adducts have a longer half-life than does 7-(oxoethyl)guanine, they have a greater potential to accumulate with long-term exposure (Swenberg *et al.* 1992). The mechanism of carcinogenicity of vinyl bromide may be similar to that of vinyl chloride (see Introduction). There is no evidence to suggest that mechanisms by which vinyl bromide causes tumors in experimental animals would not also operate in humans.

### *Cancer Studies in Humans*

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to vinyl bromide.

## Properties

Vinyl bromide is a halogenated olefin compound that exists at room temperature as a colorless gas with a characteristic pungent, but pleasant, odor. It is insoluble in water but soluble in ethanol, ether, acetone, chloroform, and benzene. It is stable under normal temperatures and pressures, but is extremely flammable (Akron 2009). Physical and chemical properties of vinyl bromide are listed in the following table.

| Property | Information |
|---|---|
| Molecular weight | 106.9[a] |
| Specific gravity | 1.4933 at 20°C[a] |
| Melting point | –137.8°C[a] |
| Boiling point | 15.8°C at 760 mm Hg[a] |
| Log $K_{ow}$ | 1.57[a] |
| Water solubility | 7.600 g/L at 25°C[b] |
| Vapor pressure | 1,033 mm Hg at 25°C[a] |
| Vapor density relative to air | 3.7[a] |

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

## Use

Vinyl bromide is used primarily in the production of polymers and copolymers. It is used in polymers as a flame retardant and in the production of monoacrylic fibers for carpet-backing material. Combined with acrylonitrile as a co-monomer, it is used to produce fabrics and fabric blends used in sleepwear (mostly children's) and home furnishings. When copolymerized with vinyl acetate and maleic anhydride, vinyl bromide is used to produce granular products. Copolymers of vinyl chloride and vinyl bromide are used to prepare films, for impregnating or laminating fibers, and as rubber substitutes. Vinyl bromide also is used in leather and fabricated-metal products. Polyvinyl bromide, made from vinyl bromide, is a polymer of little commercial value, because it is unstable at room temperature. Vinyl bromide is also used in the production of pharmaceuticals and fumigants (IARC 1986).

## Production

Vinyl bromide was first produced in the United States in 1968. U.S. production of vinyl bromide decreased from 51 million pounds in 1982 to less than 1 million pounds in 1994 (EPA 1998, HSDB 2009). In 2009, one U.S. manufacturer of vinyl bromide was identified (HSDB 2009). No more recent data on U.S. production and no data on U.S. imports or exports of vinyl bromide were found.

## Exposure

The main routes of potential exposure to vinyl bromide are inhalation and dermal contact. Vinyl bromide is not known to occur naturally in the environment, and it is assumed that most, if not all, exposure of the general population occurs as a result of industrial contamination of the environment (IARC 1986). According to EPA's Toxics Release Inventory, environmental releases of vinyl bromide between 1988 and 1997 and ranged from 1,600 lb to almost 55,000 lb. No releases were reported in 1998, and no releases have been reported since 1999, when one facility released 500 lb to air (TRI 2009).

Workers in the following industries potentially are exposed to vinyl bromide: Chemicals and Allied Production, Rubber and Plastic Production, Leather and Leather Product Production, and Fabricated Metal Production for Wholesale Trade (NIOSH 1978). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 1,821 workers potentially were exposed to vinyl bromide (NIOSH 1990). Occupational exposure to vinyl bromide (median 8-h time-weighted average) calculated for a vinyl bromide manufacturing plant ranged from 0.4 to 27.5 mg/m$^3$ (0.1 to 6.3 ppm), depending on the job and the area surveyed. Concentrations in one-hour personal air samples were 0.4 to 1.7 mg/m$^3$ (0.09 to 0.4 ppm) for a plant operator, 1.3 to 2.2 mg/m$^3$ (0.3 to 0.5 ppm) for a laboratory technician, and 5.2 to 27.5 mg/m$^3$ (1.2 to 6.3 ppm) for two loading crewmen (IARC 1986).

## Regulations

***Department of Transportation (DOT)***

Vinyl bromide is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

***Environmental Protection Agency (EPA)***

*Clean Air Act*

*National Emission Standards for Hazardous Air Pollutants:* Listed as a hazardous air pollutant.

*Comprehensive Environmental Response, Compensation, and Liability Act*

Reportable quantity (RQ) = 100 lb.

*Emergency Planning and Community Right-To-Know Act*

*Toxics Release Inventory:* Listed substance subject to reporting requirements.

## Guidelines

***American Conference of Governmental Industrial Hygienists (ACGIH)***

Threshold limit value – time-weighted average (TLV-TWA) = 0.5 ppm.

***National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)***

Listed as a potential occupational carcinogen.

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Ballering LA, Nivard MJ, Vogel EW. 1996. Characterization by two-endpoint comparisons of the genetic toxicity profiles of vinyl chloride and related etheno-adduct forming carcinogens in *Drosophila*. *Carcinogenesis* 17(5): 1083-1092.

Benya TJ, Busey WM, Dorato MA, Berteau PE. 1982. Inhalation carcinogenicity bioassay of vinyl bromide in rats. *Toxicol Appl Pharmacol* 64(3): 367-379.

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Bolt HM, Filser JG, Hinderer RK. 1978. Rat liver microsomal uptake and irreversible protein binding of [1,2-$^{14}$C]vinyl bromide. *Toxicol Appl Pharmacol* 44(3): 481-489.

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Sasaki YF, Saga A, Akasaka M, Ishibashi S, Yoshida K, Su YQ, Matsusaka N, Tsuda S. 1998. Detection of *in vivo* genotoxicity of haloalkanes and haloalkenes carcinogenic to rodents by the alkaline single cell gel electrophoresis (comet) assay in multiple mouse organs. *Mutat Res* 419(1-3): 13-20.

Swenberg JA, Fedtke N, Ciroussel F, Barbin A, Bartsch H. 1992. Etheno adducts formed in DNA of vinyl chloride-exposed rats are highly persistent in liver. *Carcinogenesis* 13(4): 727-729.

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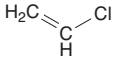
# Vinyl Chloride

## CAS No. 75-01-4

Known to be a human carcinogen

First listed in the *First Annual Report on Carcinogens* (1980)



## Carcinogenicity

Vinyl chloride is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans.

### *Cancer Studies in Humans*

The strongest evidence that vinyl chloride causes cancer in humans is based on numerous epidemiological studies and case reports that show its association with cancer of the blood vessels of the liver (hepatic angiosarcoma), which is a very rare tumor. Several studies have also reported an association between exposure to vinyl chloride and cancer at other tissue sites, including the liver (hepatocellular carcinoma), brain, lung, lymphatic system, and hematopoietic system (IARC 1987).

Since vinyl chloride was listed in the *First Annual Report on Carcinogens,* epidemiological studies have continued to provide strong evidence for an association between vinyl chloride exposure and hepatic angiosarcoma (IARC 2008). As of 1999, 197 cases of vinyl chloride–associated hepatic angiosarcoma had been reported, including 50 in the United States (Kielhorn *et al*. 2000). Two studies also found that the risk of liver cancer (hepatocellular carcinoma) increased with increasing cumulative exposure to vinyl chloride. Some studies also reported an excess of cancer of the connective and soft tissues. An excess of brain cancer was found in some but not all studies; significantly increased risks were found among exposed workers with the highest durations of exposure or who worked in plants that had begun production earlier. However, risk estimates did not increase with increasing measures of cumulative exposure, duration of exposure, or time since first exposure. The results of recent studies on lung cancer, lymphoma, and leukemia and vinyl chloride exposure were conflicting (IARC 2008).

### *Cancer Studies in Experimental Animals*

There is sufficient evidence for the carcinogenicity of vinyl chloride in experimental animals. Vinyl chloride caused tumors in three rodent species, at different several tissue sites, and by several different routes of exposure (IARC 1979). In several studies, vinyl chloride caused tumors of the blood vessels of the liver (hepatic hemangiosarcoma) in mice and rats exposed by inhalation and in rats exposed orally. Inhalation exposure to vinyl chloride also caused mammary-gland tumors in rats, mice, and hamsters; skin tumors in rats and hamsters; Zymbal-gland tumors in rats; and lung tumors in mice. Zymbal-gland cancer (carcinoma) was also observed in prenatally exposed rats. Combined inhalation exposure to vinyl chloride and oral exposure to ethanol caused more liver tumors (including angiosarcoma) than did exposure to vinyl chloride alone.

Since vinyl chloride was listed in the *First Annual Report on Carcinogens,* additional studies in rodents have been identified. Vinyl chloride administered by additional routes of exposure—perinatal (for 5 weeks beginning at birth) and prenatal followed by inhalation exposure (for 8 or 69 weeks)—also caused hepatic hemangiosarcoma (IARC 2008). Other studies reported that exposure to vinyl chloride caused tumors at additional tissue sites. Inhalation exposure to vinyl chloride caused hemangiosarcoma not only in the liver, but at sites other than the liver in rats, mice, and hamsters. Inhalation exposure also caused stomach tumors (adenoma) in hamsters and nasal and kidney tumors in rats. Liver cancer (hepatocellular carcinoma) was observed in rats after inhalation exposure, perinatal exposure, or prenatal exposure followed by inhalation exposure.

### *Studies on Mechanisms of Carcinogenesis*

Vinyl chloride is metabolized by cytochrome P450 enzymes to form chloroethylene oxide, which can undergo spontaneous rearrangement to form chloracetaldehyde; both of these metabolites can bind to DNA. One major DNA adduct, 7-(2′-oxoethyl)guanine, and four minor adducts (etheno adducts) have been identified. The etheno adducts (but not the major adduct) cause mutations, mainly base-pair substitutions and, to a lesser degree, frameshift mutations. Mutations were detected in the *p53* tumor-suppressor gene and the *ras* proto-oncogene in angiosarcomas from humans and angiosarcomas of the liver or hepatocellular carcinomas from rats exposed to vinyl chloride. Most of the mutations occurred at A:T base pairs, which is consistent with the mutagenic properties of the etheno adducts (especially the 1,$N^6$-ethenoadenine adduct) (Kielhorn *et al*. 2000).

Vinyl chloride caused genetic damage in many test systems, including bacteria, yeast, insects, cultured human and other mammalian cells, and rodents exposed *in vivo,* and in exposed humans. The genetic damage included mutations, DNA damage, micronucleus formation, chromosomal aberrations, and sister chromatid exchange. Vinyl chloride caused mutations in bacteria with or without metabolic activation (addition of rodent liver microsomes to simulate mammalian metabolism); however, its metabolites chloroethylene oxide and chloracetaldehyde were more potent mutagens than vinyl chloride. These results suggest that vinyl chloride may require mammalian metabolic activation in order to cause genetic damage in other test systems (Giri 1995).

## Properties

Vinyl chloride is a halogenated olefin compound that exists at room temperature as a colorless gas with an ethereal odor. It is slightly soluble in water and soluble in most organic solvents, including alcohol, ether, benzene, carbon tetrachloride and other chlorinated solvents, hydrocarbons, and oils. It is very flammable and polymerizes in light or the presence of a catalyst (IARC 1979). Physical and chemical properties of vinyl chloride are listed in the following table.

| Property | Information |
|---|---|
| Molecular weight | 62.5[a] |
| Specific gravity | 0.9106 at 20°C/4°C[a] |
| Melting point | –153.7°C[a] |
| Boiling point | –13.3°C[a] |
| Log $K_{ow}$ | 1.62[b] |
| Water solubility | 8.8 g/L at 25°C[b] |
| Vapor pressure | 2980 mm Hg at 25°C[a] |
| Vapor density relative to air | 2.15[a] |

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

## Use

Vinyl chloride is used almost exclusively by the plastics industry to produce polyvinyl chloride (PVC) and copolymers. PVC is a plastic resin used in many consumer and industrial products, including automotive parts and accessories, furniture, medical supplies, containers, wrapping film, battery cell separators, electrical insulation, water-distribution systems, flooring, windows, videodiscs, irrigation systems, and credit cards. More than 95% of all vinyl chloride monomer produced is used to make PVC and its copolymers; the rest is used in organic synthesis and miscellaneous applications (Kielhorn

*et al.* 2000, HSDB 2009). Vinyl chloride–vinyl acetate copolymers are used extensively to produce films and resins (IARC 1974, 1979, NCI 1978, ATSDR 2006). Vinyl chloride previously was used as a refrigerant, as an extraction solvent, and in aerosol propellants, but these uses were banned in 1974 because of vinyl chloride's carcinogenic effects (HSDB 2009).

## Production

Vinyl chloride was first produced commercially in the 1920s and became one of the highest-volume chemicals produced in the United States, ranking 17th or 18th in production volume during the mid 1990s (Kirschner 1996). In 2009, eight U.S. suppliers of vinyl chloride were identified (ChemSources 2009). Annual U.S. production increased from 6 billion pounds in the late 1970s to 15 billion pounds in the mid1990s (Kirschner 1996, HSDB 2009). In 2015, combined U.S. production and imports exceeded 10 billion pounds (as shown in the table below). From 1989 to 2009, annual U.S. imports of vinyl chloride declined from 302 million pounds to 818,000 lb (ATSDR 2006, USITC 2009). In 2017, imports totaled less than 2 million pounds, accounting for less than 0.02% of U.S. production. U.S. exports of vinyl chloride were 2.2 billion pounds in 2000 and 2.3 billion pounds in 2009 (USITC 2009), similar to the volume reported for 2017, which accounted for no more than one third of total U.S. production plus imports.

| Category | Year | Quantity (lb) |
|---|---|---|
| Production + imports[a] | 2015 | 10 billion to 20 billion |
| U.S. imports[b] | 2017 | 1.8 million |
| U.S. exports[b] | 2017 | 2.8 billion |

Sources: [a]EPA 2016. [b]USITC 2018.

## Exposure

The general population potentially is exposed to vinyl chloride through inhalation of contaminated air, ingestion of contaminated drinking water and foods, or dermal contact with consumer products. However, the exposure levels for the majority of the population are very low (Kielhorn *et al.* 2000, ATSDR 2006, HSDB 2009). In the past, vinyl chloride was detected in various foods and beverages that were packaged in materials made of PVC; however, U.S. Food and Drug Administration regulations have essentially eliminated this route of exposure. The estimated average daily intake of vinyl chloride from the diet is essentially zero (ATSDR 2006). Vinyl chloride has also been detected in domestic and foreign cigarettes and little cigars at levels ranging from 5.6 to 27 ng per cigarette and in a marijuana cigarette at 5.4 ng (IARC 1979).

Vinyl chloride is released into the environment in emissions and effluents from the plastics industry (ATSDR 2006). According to the U.S. Environmental Protection Agency's Toxics Release Inventory, annual environmental releases of vinyl chloride declined slowly from 1.4 million pounds in 1988 to less than 1 million pounds since 1998. In 2007, 43 facilities released 373,000 lb of vinyl chloride, mostly to air (TRI 2009). Segments of the general population living near emission sources potentially are exposed to relatively high levels of vinyl chloride in air. Concentrations in the air near emission sources ranged from trace levels to over 2,600 μg/m$^3$, and the average daily intake of vinyl chloride by residents living near emission sources ranged from trace amounts to 2,100 μg. Ambient air in rural and urban areas of the United States typically does not contain detectable levels of vinyl chloride. The majority of the population is not expected to be exposed to vinyl chloride in drinking water. Only 7 of 945 water supplies sampled throughout the United States contained detectable levels of vinyl chloride. In another study, vinyl chloride was detected in only 12 of 11,202 public water supplies using surface waters as their primary source. EPA estimated that about 0.9% of the U.S. population was exposed to vinyl chloride in drinking water at concentrations of 1.0 μg/L or higher and that 0.3% was exposed at concentrations higher than 5 μg/L (ATSDR 2006).

Potential routes of occupational exposure to vinyl chloride are inhalation and dermal contact. Occupational exposure generally occurs after production, when the finished monomer is piped to storage or transportation, or during maintenance. The potential for exposure is high during the process of polymerization to form PVC resins or other materials, because vinyl chloride monomer may escape into the air (NCI 1978). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 81,314 workers potentially were exposed to vinyl chloride (ATSDR 2006).

## Regulations

***Coast Guard (Dept. of Homeland Security)***

Minimum requirements have been established for safe transport of vinyl chloride on ships, barges, and self-propelled vessels.

***Consumer Product Safety Commission (CPSC)***

Self-pressurized products intended for household use that contain vinyl chloride are banned.

***Department of Transportation (DOT)***

Vinyl chloride is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

***Environmental Protection Agency (EPA)***

*Clean Air Act*

*National Emission Standards for Hazardous Air Pollutants:* Listed as a hazardous air pollutant.
*New Source Performance Standards:* Manufacture of vinyl chloride is subject to certain provisions for the control of volatile organic compound emissions.
*Prevention of Accidental Release:* Threshold quantity (TQ) = 10,000 lb.
*Urban Air Toxics Strategy*: Identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

*Clean Water Act*

*Effluent Guidelines:* Listed as a toxic pollutant.
*Water Quality Criteria:* Based on fish or shellfish and water consumption = 0.22 μg/L; based on fish or shellfish consumption only = 1.6 μg/L.

*Comprehensive Environmental Response, Compensation, and Liability Act*

Reportable quantity (RQ) = 1 lb.

*Emergency Planning and Community Right-To-Know Act*

*Toxics Release Inventory:* Listed substance subject to reporting requirements.

*Resource Conservation and Recovery Act*

*Characteristic Hazardous Waste:* Toxicity characteristic leaching procedure (TCLP) threshold = 0.2 mg/L.
*Listed Hazardous Waste:* Waste codes for which the listing is based wholly or partly on the presence of vinyl chloride = U043, K019, K020, K028, K029.
Listed as a hazardous constituent of waste.

*Safe Drinking Water Act*

Maximum contaminant level (MCL) = 0.002 mg/L.

***Food and Drug Administration (FDA, an HHS agency)***

Maximum permissible level in bottled water = 0.002 mg/L.
Aerosol drug products containing vinyl chloride have been withdrawn from the market and may not be compounded, because vinyl chloride was found to be unsafe or not effective.
Vinyl chloride is banned from use in cosmetic aerosol products.

***Occupational Safety and Health Administration (OSHA, Dept. of Labor)***

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2018, specific PELs may not reflect the more current studies and may not adequately protect workers.
Permissible exposure limit (PEL) = 1 ppm.
Ceiling concentration = 5 ppm (15 min).
Comprehensive standards have been developed for occupational exposure to vinyl chloride.

## Guidelines

***American Conference of Governmental Industrial Hygienists (ACGIH)***

Threshold limit value – time-weighted average (TLV-TWA) = 1 ppm.

***National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)***

Listed as a potential occupational carcinogen.

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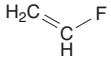
# Vinyl Fluoride

## CAS No. 75-02-5

Reasonably anticipated to be a human carcinogen

First listed in the *Tenth Report on Carcinogens* (2002)

Also known as fluoroethene



## Carcinogenicity

Vinyl fluoride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

### *Cancer Studies in Experimental Animals*

Exposure to vinyl fluoride by inhalation caused tumors at several different tissue sites in rats and mice. In rats and mice of both sexes, it caused cancer of the blood vessels of the liver (hepatic hemangiosarcoma). In rats of both sexes, it also caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma) and cancer of the Zymbal gland (carcinoma). In mice, it also caused benign or malignant lung tumors (bronchiolar/alveolar adenoma or adenocarcinoma) and benign Harderian-gland tumors (adenoma) in both sexes and mammary-gland cancer (adenocarcinoma) in females (Bogdanffy *et al.* 1995, IARC 1995).

### *Studies on Mechanisms of Carcinogenesis*

Vinyl fluoride caused mutations in *Salmonella typhimurium* in the presence of mammalian metabolic activation. It also caused gene mutations and chromosomal aberrations in Chinese hamster ovary cells (with metabolic activation), sex-linked recessive lethal mutations in *Drosophila melanogaster*, and micronucleus formation in bone-marrow cells of female mice (IARC 1995).

Vinyl fluoride 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 vinyl fluoride at similar rates (Cantoreggi and Keller 1997). Vinyl fluoride metabolites form covalent DNA adducts. Inhalation exposure of rats and mice to vinyl fluoride caused a dose-related increase in the formation of the promutagenic adduct $N^2$,3-ethenoguanine in liver DNA (Swenberg *et al.* 1995). The mechanism of carcinogenicity of vinyl fluoride may be similar to that of vinyl chloride (see Introduction). There is no evidence to suggest that mechanisms by which vinyl fluoride causes tumors in experimental animals would not also operate in humans.

### *Cancer Studies in Humans*

No epidemiological studies have evaluated the relationship between human cancer and exposure specifically to vinyl fluoride.

## Properties

Vinyl fluoride is a halogenated olefin compound that exists at room temperature as a colorless gas with a faint ethereal odor. It is slightly soluble in water, and soluble in alcohol, ether, and acetone. It polymerizes freely and forms explosive mixtures with air (IARC 1986). Physical and chemical properties of vinyl fluoride are listed in the following table.

| Property | Information |
|---|---|
| Molecular weight | 46.0[a] |
| Specific gravity | 0.636 (liquid) at 21°C[a] |
| Melting point | –160.5°C[a] |
| Boiling point | –72°C[a] |
| Log $K_{ow}$ | 1.19[a] |
| Water solubility | 12.9 g/L at 25°C[b] |
| Vapor pressure | 0.414 mm Hg at 25°C[a] |
| Vapor density relative to air | 1.58[a] |

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

## Use

Vinyl fluoride is used primarily in the production of polyvinyl fluoride and other fluoropolymers. Polymers of vinyl fluoride are resistant to weather and exhibit 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

Vinyl fluoride was first prepared in the early 1900s by reaction of zinc with 1,1-difluoro-2-bromoethane. Modern preparation of vinyl fluoride involves reaction of acetylene and hydrogen fluoride in the presence of a mercury-based or aluminum-based catalyst (IARC 1995). In 2009, one U.S. manufacturer of vinyl fluoride was identified (HSDB 2009). Annual U.S. production of vinyl fluoride from the 1970s to 1990 ranged from 1 million to 3.3 million pounds (EPA 2006,

HSDB 2009). No more recent data on U.S. production and no data on U.S. imports or exports of vinyl fluoride were found.

## Exposure

Exposure to vinyl fluoride in the environment will occur by inhalation, because vinyl fluoride is released into the environment as a gas (IPCS 1993). Occupational exposure to vinyl fluoride also occurs primarily by inhalation (HSDB 2009). Skin and eye contact can occur among workers handling liquid vinyl fluoride. Handling of liquid vinyl fluoride also would cause frostbite (IPCS 1993). Occupational exposure to vinyl fluoride was studied in a manufacturing and polymerization facility in the United States. In eight personal air samples taken at the manufacturing facility, concentrations of vinyl fluoride generally were less than 2 ppm (3.76 mg/m$^3$). In one personal sample, however, the concentration was 21 ppm (39.5 mg/m$^3$). Vinyl fluoride 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 vinyl fluoride concentrations ranged from 1 to 5 ppm (1.88 to 9.4 mg/m$^3$) (IARC 1995).

## Regulations

***Department of Transportation (DOT)***

Vinyl fluoride is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

***Environmental Protection Agency (EPA)***

*Clean Air Act*

*Prevention of Accidental Release:* Threshold quantity (TQ) = 10,000 lb.

*Emergency Planning and Community Right-To-Know Act*

*Toxics Release Inventory:* Listed substance subject to reporting requirements.

## Guidelines

***American Conference of Governmental Industrial Hygienists (ACGIH)***

Threshold limit value – time-weighted average (TLV-TWA) = 1 ppm.

***National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)***

Recommended exposure limit (REL) = 1 ppm.
Ceiling recommended exposure limit = 5 ppm.

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