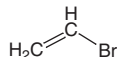


Vinyl Bromide

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 in experimental animals. Both male and female rats exposed to vinyl bromide by inhalation showed increased incidences of hepatic hemangiosarcoma, Zymbal gland carcinoma, liver neoplastic nodules, and hepatocellular carcinoma (Benya *et al.* 1982, IARC 1986).

The tumor responses of laboratory animals to vinyl bromide are similar to their responses to vinyl chloride, a known human carcinogen (IARC 1987), and to vinyl fluoride, a probable human carcinogen (IARC 1995). 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. Vinyl bromide appears to be a more potent inducer of liver hemangiosarcoma in rats than is vinyl chloride. The fact that vinyl bromide, vinyl chloride, and vinyl fluoride 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 vinyl bromide and human cancer were found

Additional Information Relevant to Carcinogenicity

Vinyl bromide is genotoxic in *Salmonella typhimurium* (IARC 1986) and *Drosophila melanogaster* (Ballering *et al.* 1996) and induces 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 metabolizes more slowly than does vinyl chloride (Km for vinyl bromide metabolism is approximately an order of magnitude lower) (Bolt *et al.* 1978), which suggests that vinyl bromide's greater carcinogenic potency may be related to kinetic differences in metabolism.

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) (Bolt 1988). 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/RNA adducts (1,N⁶-ethenoadenosine and 3,N⁴-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-(2-oxoethyl)guanine, they have a greater potential to accumulate with long-term exposure (Swenberg *et al.* 1992).

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

Properties

Vinyl bromide is a colorless, highly flammable gas with a characteristic pungent odor. It is insoluble in water and soluble in chloroform, 10%

ethanol, 10% ethyl ether, 10% acetone, and 10% benzene. It reacts with strong oxidizing agents, copper, copper alloys, and plastics (IARC 1986).

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 also is used in the production of pharmaceuticals and fumigants (IARC 1986).

Production

Vinyl bromide was first produced in the United States in 1968. In 1982, U.S. production was estimated to be approximately 51 million lbs. Vinyl bromide was not listed as a high production volume chemical in 1994, indicating that annual production was less than 1 million lb (EPA 1994). The Hazardous Substances Data Bank identified one U.S. manufacturer (HSDB 2001).

Exposure

Exposure to vinyl bromide in the environment will occur primarily by inhalation and dermal contact. Vinyl bromide is not known to occur naturally in the environment. It is assumed that most, if not all, vinyl bromide environmental exposure occurs as a result of industrial contamination (IARC 1986).

In 1999, only one facility reported environmental releases of vinyl bromide, consisting of 500 lb released into the air. No environmental releases were reported to the EPA's Toxics Release Inventory in 1998; however, environmental releases ranged from approximately 1,600 to almost 55,000 lb between 1988 and 1997 (HSDB 2001).

The National Institute for Occupational Safety and Health (NIOSH) has identified the following industries in which vinyl bromide exposure occurs: chemicals and allied production, rubber and plastic production, leather and leather product production, and fabricated metal production for wholesale trade (NIOSH 1978). The NIOSH National Occupational Exposure Survey estimated that 1,821 workers potentially were exposed to vinyl bromide between 1981 and 1983 (HSDB 2001).

Vinyl bromide occupational exposures (median 8-hour time-weighted average) calculated for a vinyl bromide manufacturing plant ranged from 0.4 to 27.5 mg/m³ (0.1 to 6.3 ppm), depending on the job and the area surveyed. Personal air samples (one hour) showed that a plant operator was exposed to 0.4 to 1.7 mg/m³ (0.09 to 0.4 ppm), a laboratory technician to 1.3 to 2.2 mg/m³ (0.3 to 0.5 ppm), and two loading crewmen to 5.2 to 27.5 mg/m³ (1.2 to 6.3 ppm) vinyl bromide (IARC 1986).

Regulations

DOT

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

EPA

Clean Air Act

NESHAP: Listed as a Hazardous Air Pollutant (HAP)

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

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 0.5 ppm

NIOSH

Listed as a potential occupational carcinogen

REFERENCES

- Ballering, L. A., M. J. Nivard and E. W. Vogel. 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): 1083-92.
- Benya, T. J., W. M. Busey, M. A. Dorato and P. E. Berteau. 1982. Inhalation carcinogenicity bioassay of vinyl bromide in rats. *Toxicol Appl Pharmacol* 64(3): 367-79.
- Bolt, H. M. 1988. Roles of etheno-DNA adducts in tumorigenicity of olefins. *Crit Rev Toxicol* 18(4): 299-309.
- Bolt, H. M., J. G. Filser and R. K. Hinderer. 1978. Rat liver microsomal uptake and irreversible protein binding of [1,2-14C]vinyl bromide. *Toxicol Appl Pharmacol* 44(3): 481-9.
- EPA. 1994. Vinyl Bromide. U.S. Environmental Protection Agency. <http://www.epa.gov/opptintr/chemrtk/opptsrch.htm> and search 593-60-2.
- Guengerich, F. P., P. S. Mason, W. T. Stott, T. R. Fox and P. G. Watanabe. 1981. Roles of 2-haloethylene oxides and 2-haloacetaldehydes derived from vinyl bromide and vinyl chloride in irreversible binding to protein and DNA. *Cancer Res* 41(11 Pt 1): 4391-8.
- HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
- IARC. 1986. Some Chemicals Used in Plastics and Elastomers. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 39. Lyon, France: International Agency for Research on Cancer. 403 pp.
- IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.
- IARC. 1995. Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 63. Lyon, France: International Agency for Research on Cancer. 558 pp.
- NIOSH. 1978. Current Intelligence Bulletin 28. Joint NIOSH/OSHA. Vinyl Halides - Carcinogenicity. Vinyl Bromide, Vinyl Chloride and Vinylidene Chloride. National Institute for Occupational Safety and Health. http://www.cdc.gov/niosh/79102_28.html.
- Sasaki, Y. F., A. Saga, M. Akasaka, S. Ishibashi, K. Yoshida, Y. Q. Su, N. Matsusaka and S. Tsuda. 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, J. A., N. Fedtke, F. Ciroussel, A. Barbin and H. Bartsch. 1992. Etheno adducts formed in DNA of vinyl chloride-exposed rats are highly persistent in liver. *Carcinogenesis* 13(4): 727-9.