VINYL BROMIDE

Data were last reviewed in IARC (1986) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Services Reg. No.: 593-60-2
Chem. Abstr. Name: Bromoethene
IUPAC Systematic Name: Bromoethylene

1.1.2 *Structural and molecular formulae and relative molecular mass*

C_2H_3Br Relative molecular mass: 106.96

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Colourless gas with a characteristic pungent odour; colourless liquid under pressure (American Conference of Governmental Industrial Hygienists, 1992)
(*b*) *Boiling-point*: 15.8°C (Lide, 1997)
(*c*) *Melting-point*: –137.8°C (Lide, 1997)
(*d*) *Density*: 1.522 at 20°C (Lide, 1997)
(*e*) *Solubility*: Insoluble in water; soluble in acetone, benzene, chloroform and ethanol; very soluble in diethyl ether (American Conference of Governmental Industrial Hygienists, 1992; Lide, 1997)
(*f*) *Vapour pressure*: 119 kPa at 20°C; relative vapour density, 3.7 (American Conference of Governmental Industrial Hygienists, 1992)
(*g*) *Explosive limits*: Upper, 15%; lower, 9% by volume (United States National Library of Medicine, 1998a)
(*h*) *Conversion factor*: $mg/m^3 = 4.37 \times ppm$

1.2 Production and use

Information available in 1995 indicated that vinyl bromide was produced in three countries (Germany, Japan and the United States) (Chemical Information Services, Inc., 1995).

Vinyl bromide has been used as an intermediate in organic synthesis and in the manufacture of polymers, copolymers, flame retardants, pharmaceuticals and fumigants (American Conference of Governmental Industrial Hygienists, 1992).

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997; United States National Library of Medicine, 1998b), approximately 1822 workers in the United States were potentially exposed to vinyl bromide (see General Remarks).

1.3.2 *Environmental occurrence*

Vinyl bromide may form in air as a degradation product of 1,2-dibromoethane. It may also be released to the environment from facilities which manufacture or use vinyl bromide as a flame retardant for acrylic fibres. Vinyl bromide has been qualitatively identified in ambient air samples (United States National Library of Medicine, 1998a)

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 22 mg/m^3 as the 8-h time-weighted average threshold limit value, with an animal carcinogen notation, for occupational exposures to vinyl bromide in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for vinyl bromide in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Vinyl bromide was tested for carcinogenicity in female mice by skin application and by subcutaneous injection, and in rats by inhalation exposure. In the inhalation study in rats, there was a dose-related increase in the incidence of liver angiosarcomas and Zymbal gland carcinomas; an increased incidence of liver neoplastic nodules and hepatocellular carcinoma was also noted. In the limited studies in mice by skin application and subcutaneous administration, no local tumour was observed (IARC, 1986).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

Vinyl bromide is readily absorbed upon inhalation by rats and showed an 11-fold accumulation within the rats compared with the concentration in gaseous phase. Metabolism is saturable at exposure concentrations greater than 250 mg/m^3. Following inhalation of vinyl bromide by rats, rabbits and monkeys, plasma levels of nonvolatile bromide increased with exposure duration, and more rapidly in phenobarbital-pretreated rats.

A volatile alkylating metabolite was formed in a mouse-liver microsomal system. The primary metabolite formed *in vitro* by mixed function oxidases is 2-bromoethylene oxide, which rearranges to 2-bromoacetaldehyde.

In rats, the conversion of vinyl bromide to reactive metabolites occurs primarily in hepatocytes. Irreversible binding of such metabolites to proteins and RNA has been established both with rat-liver microsomes *in vitro* and in rats in *vivo*. They can also alkylate the cytochrome P450 prosthetic group of phenobarbital-treated rat-liver microsomes. Exposure of rats to vinyl bromide causes a decrease in hepatic cytochrome P450 (IARC, 1986).

4.2 Toxic effects

4.2.1 *Humans*

Vinyl bromide inhalation is reported to cause loss of consciousness. It is a skin and eye irritant and causes a 'frost-bite' type of burn (IARC, 1986).

4.2.2 *Experimental systems*

Subacute inhalation studies performed with rats, rabbits and monkeys showed no significant haematological, gross pathological or histopathological change. Vinyl bromide is far less hepatotoxic than vinyl chloride in rats. However, its hepatotoxicity is enhanced in rats pretreated with polychlorinated biphenyls, as demonstrated by enzymatic and histological signs of liver damage. Like other halogenated compounds transformed to reactive metabolites, vinyl bromide alters rat intermediary metabolism, leading to acetone exhalation (IARC, 1986).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects (see Table 1 for references)

Vinyl bromide is mutagenic to *Salmonella typhimurium* and induced somatic mutations in *Drosophila melanogaster*. It is considered that vinyl bromide reacts with DNA to form various etheno-adducts which are the same as those formed by vinyl chloride (Bolt *et al.*, 1986).

Table 1. Genetic and related effects of vinyl bromide

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SAF, *Salmonella typhimurium* BA13/BAL13, forward mutation, arabinoside resistance	+	+	15190	Roldán-Arjona *et al*. (1991)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	1% in air	Lijinsky & Andrews (1980)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	+	0.2% in air	Bartsch *et al*. (1979)
DMM, *Drosophila melanogaster*, somatic mutation (*white/white*$^+$)	+		4000 ppm in air	Vogel & Nivard (1993)
DMM, *Drosophila melanogaster*, somatic mutation (*white/white*$^+$)	+		2000 ppm in air	Rodriguez-Arnaiz *et al*. (1993)

[a] +, positive
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Occupational exposure may occur during the production of vinyl bromide and its polymers.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

Vinyl bromide was tested in female mice by skin application and by subcutaneous injection, and in rats by inhalation exposure. In the inhalation study in rats, there was a dose-related increase in the incidence of liver angiosarcomas and Zymbal gland carcinomas; an increased incidence of liver neoplastic nodules and hepatocellular carcinoma was also noted.

5.4 Other relevant data

Vinyl bromide was mutagenic to *Salmonella typhimurium* and *Drosophila melanogaster*.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of vinyl bromide were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of vinyl bromide.

Overall evaluation

Vinyl bromide is *probably carcinogenic to humans (Group 2A)*.

In making the overall evaluation, the Working Group took into consideration that all available studies showed a consistently parallel response between vinyl bromide and vinyl chloride. In addition, both vinyl chloride and vinyl bromide are activated via a P450-dependent pathway to their corresponding epoxides. For both vinyl chloride and vinyl bromide, the covalent binding of these compounds to DNA forms the respective etheno adducts. The weight of positive evidence for both compounds was also noted among the studies for genotoxicity, although the number and variety of tests for vinyl bromide were fewer.

6. References

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