VINYL BROMIDE

CAS number: 593-60-2

Synonyms: Bromoethene, bromoethylene, ethylene bromo

Chemical formula: C_2H_3Br

Workplace exposure standard (interim)

TWA: **0.5 ppm (2.2 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **Carc. 1B**

IDLH: **—**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.5 ppm (2.2 mg/m^3) is recommended in the interim to protect for the risk of cancer in exposed workers.

A priority review of the data in the next scheduled review of the workplace exposure standards is recommended.

Discussion and conclusions

Vinyl bromide is used primarily in polymers as a flame retardant in the production of acrylic fibres for carpet-backing material. It is also used as an intermediate in organic synthesis and in the manufacture of polymers, copolymers, flame retardants, pharmaceuticals and fumigants.

The critical effect of exposure is cancer.

No human studies of vinyl bromide toxicity are available. Treatment-related increases in liver angiosarcomas and Zymbal gland squamous cell carcinomas was reported in all the exposed groups in a two-year inhalation study in rats exposed at 0, 10, 50, 250 or 1,250 ppm. Statistically significant increase in hepatocellular adenomas and carcinomas was also observed in some dose groups. Vinyl bromide caused DNA damage in mice treated *in vivo* and has been reported to be mutagenic in bacteria. Metabolites formed DNA adducts as in vinyl chloride. It has been suggested that the chemical may be a more potent carcinogen than vinyl chloride (ACGIH, 2018; SCOEL, 2008). SCOEL (2008) and NICNAS (2016) cite the critical effects to humans as carcinogenicity and genotoxicity and IARC (2008) class it as probably carcinogenic to humans. For the purposes of this assessment, vinyl bromide is assumed to be a non-threshold-based genotoxic carcinogen.

No appropriate inhalation unit risk or slope factor is available to calculate a risk-based TWA. As such, an interim TWA of 0.5 ppm, cited by the ACGIH (2018) as protective of the cancer endpoint, is recommended. A priority assessment in the next review of the workplace exposure standards is recommended.

Recommendation for notations

Classified as a carcinogen category 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 5 ppm (22 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 0.5 ppm (2.2 mg/m^3)***

TLV-TWA intended to minimise potential for liver cancer, observed in rodents exposed at 10 ppm; by analogy with vinyl chloride.

Summary of data:

- No human toxicity studies available
- Structurally like vinyl chloride, a known human carcinogen
- Carcinogenicity studies in rats for vinyl bromide and vinyl chloride indicate vinyl bromide is a more potent carcinogen at equivalent exposure levels
- Vinyl bromide metabolised to 2-bromoethylene oxide, which is structurally similar to mutagenic vinyl chloride metabolite 2-chloroethylene oxide, by both rat and human liver microsomal preparations
- Vinyl bromide is metabolised *in vitro* ≈50% faster than vinyl chloride at saturating concentrations of substrate
- No case of angiosarcoma associated with occupational exposure to vinyl chloride in the USA since introduction of TLV-TWA of 1 ppm in 1974
- As vinyl bromide may be a more potent carcinogen than vinyl chloride, a TLV–TWA of 0.5 ppm is recommended.

Human data:

- High concentrations produce dizziness, disorientation and sleepiness in humans (no further information)
- Liquid contact to eyes or skin cause irritation as well as frost bite due to rapid evaporation.

Animal data:

- Results of studies in rats exposed 6 h/d, 5 d/wk for 2 yr at 0, 10, 50, 250 or 1,250 ppm by inhalation include:
  - decrease in body weight at all exposure concentrations
  - cumulative mortality followed correlated with 50, 250 and 1,250 ppm but not at 10 ppm
  - angiosarcomas, primarily of the liver, caused in both male and female rats in all 4 exposure groups
  - incidences of liver angiosarcoma in the 0, 10, 50, 250 and 1250 ppm groups were 0/144, 7/120, 36/120, 61/120 and 43/120, respectively, among males
  - primary angiosarcomas also found in lung, spleen, nasal cavity and mesentery
  - increased incidence of primary hepatocellular neoplasms seen in males exposed at 250 ppm and in females exposed at 10, 50 and 250 ppm
  - decreasing dose-response relationship at highest dose for each of the tumour sites attributed to early mortality and termination of rats in the 1250 ppm group at 72 wk
- Exposure-dependent increases in ATPase-deficient foci in hepatocytes in newborn rats exposed at 2000 ppm 8 h/d, 5 d/wk from their first day of life up to 15 wk of age.

Genotoxicity

Source	Year set	Standard

		• Mutagenic to *S. typhimurium* strains TA1530 and TA100 and tradescantia strains in the presence or absence of rat, mouse or human metabolic activation systems
		• A dose-dependent increase in the number of revertants per plate observed in *S. typhimurium* strains TA1530 or TA100 in the presence of liver S9 from phenobarbital-treated mice with or without cofactors for a NADPH generating system
		• A direct-acting mutagen in TA1530:
		  ○ the addition of mouse liver S9 enhanced the mutagenic effect, indicating a microsome-dependent formation of metabolites which are more mutagenic than the parent compound
		• S9 preparations from human liver specimens active in converting vinyl bromide to mutagens in *S. typhimurium* strains TA1530 or TA100:
		  ○ the average activity was lower than that in rats
		• More potent than vinyl chloride in causing mutations in *S. typhimurium* and in forming adducts.
		
		Insufficient data to assign a skin or sensitiser notation of TLV-STEL.

DFG	***NA***	***NA***
No report.		
SCOEL	***2008***	***Not assigned***

Summary of additional data:
• No local tumours in mice injected subcutaneously with 25 mL 1/wk for 48 wk and observed up to 420 d:
  ○ examination of animals for pathological lesions limited to the injection site
• Applied to the skin of 30 female mice at 15 mg (in 0.1 mL acetone) 3/wk for 60 wk:
  ○ no skin tumours observed
  ○ sites other than skin not examined and test material volatile
• Refers to 2 yr rat inhalation study cited by ACGIH (2018)
• Considered clearly carcinogenic in experimental animals
• Concludes that occupationally relevant low exposure range appears to be ≈3 times more active than vinyl chloride
• Quantitative assessment of available data and use of PBPK modelling infers inhalation exposure for working lifetime to 1 ppm the hepatic angiosarcoma risk of $9x10^{-4}$.		

OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2016	• Mutagenic in *S. typhimurium*

Source		Year	Additional information
			• In a comet assay in male mice, 2,000 mg/kg induced statistically significant DNA damage in all examined organs (stomach, liver, kidney, bladder, lung and brain) except bone marrow • Refers to 2-yr inhalation study in rats (ACGIH, 2018) • Critical health effects include systemic long-term effects - carcinogenicity and mutagenicity.
IARC	✓	2008	• In limited studies in female mice, neither induced nor initiated skin tumours after dermal application and did not cause injection-site tumours after repeated subcutaneous injection • In an inhalation study in rats, dose-related increase in the incidence of liver angiosarcomas and Zymbal gland carcinomas, liver neoplastic nodules; hepatocellular carcinoma also noted • Bromoethylene oxide and bromoacetaldehyde are known metabolites that form DNA adducts similar to those formed by metabolites of vinyl chloride • No epidemiological data relevant to carcinogenicity of vinyl bromide available • Sufficient evidence in experimental animals for carcinogenicity • Probably carcinogenic to humans (Group 2A) • Overall evaluation, Working Group took into consideration that all available studies showed a consistently parallel response between vinyl bromide and vinyl chloride • For practical purposes should be considered to act similarly to the human carcinogen vinyl chloride.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
Is the chemical carcinogenic with a mutagenic mechanism of action?	Yes
The chemical is a non-threshold based genotoxic carcinogen.	
Is a cancer slope factor or inhalation unit risk value available?	No

Notations

Source	Notations
SWA	Carc. 1B
HCIS	Carcinogenicity – category 1B
NICNAS	NA
EU Annex	NA
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A2

Source	Notations
DFG	NA
SCOEL	Carcinogenicity – A
HCOTN	NA
IARC	Carcinogenicity – Group 2A
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Insufficient evidence to recommend a skin notation.

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	106.95
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.45 mg/m^3; 1 mg/m^3 = 0.23 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

European Chemicals Agency (ECHA) (2019) Vinyl bromide – REACH assessment.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2008) Recommendation from the Scientific Committee on Occupational Exposure Limits for vinyl bromide. SCOEL/SUM/155.

International Agency for Research on Cancer (IARC) (2008) Vinyl bromide. IARC Monographs on the evaluation of the carcinogenic risk to humans.

NICNAS (2016) Ethene, bromo-: Human health tier II assessment