

ETHYL BROMIDE

CAS number: 74-96-4

Synonyms: Bromic ether, bromoethane, hydrobromic ether, monobromoethane

Chemical formula: C₂H₅Br

Structural formula: —

Workplace exposure standard (interim)

TWA: 5 ppm (22 mg/m³)

STEL: —

Peak limitation: —

Notations: Carc 2, Sk.

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 5 ppm (22 mg/m³) is recommended to reduce the risk of cancer and other adverse systemic effects in exposed workers.

A priority evaluation of the available data is recommended at the next scheduled review.

Discussion and conclusions

Ethyl bromide is used as an ethylating agent and solvent in the chemical and pharmaceutical industries and has been used as a refrigerant.

There are limited epidemiological data available. There is evidence to suggest carcinogenicity in experimental animals and inconclusive results in mutagenic assays. A mechanism for carcinogenicity in animals has not been established. The relevance to carcinogenicity in humans remains unclear (ACGIH, 2018; NICNAS, 2015; NTP, 1989; US EPA, 1988).

A two-year inhalation study in rats and mice noted no significant incidence of adverse effects at 100 ppm and 200 ppm. At 400 ppm tumours in various organs were identified as well as conjunctivitis, pulmonary inflammation and decrease body weights (ACGIH, 2018).

Due to residual uncertainty regarding the data, the TWA of 5 ppm is recommended in the interim to protect for systemic effects based on the recommendation by ACGIH (2018).

Given the absence of suitable data about carcinogenicity, a further review of the literature should be undertaken at the next scheduled review.

Recommendation for notations

Classified as a category 2 carcinogen 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.

A skin notation is recommended based on evidence of dermal absorption in humans and potential systemic carcinogenic effects.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 5 ppm (22 mg/m³)
ACGIH	2001	TLV-TWA: 5 ppm (22 mg/m³)
<p>TLV-TWA recommended to minimise the potential for adverse liver, kidney and cardiac effects and possible cancer.</p> <p>Summary of data:</p> <p>No derivation of TWA provided.</p> <p>Human data:</p> <ul style="list-style-type: none"> • No detailed epidemiological or human toxicological studies presented • Historically used as anaesthetic with procedural exposures reaching ≈100,000 ppm • Initial increase in pulse rate, followed by a slowed pulse and marked vasodilation; CNS depression, narcosis and anaesthesia • Fatalities have occurred from respiratory or cardiac arrest immediately following anaesthesia or up to 24 h post-treatment • A single prolonged skin exposure can lead to the absorption of harmful amounts. <p>Animal data:</p> <ul style="list-style-type: none"> • LC₅₀: 2,723 ppm (female rats) • Autopsy of the animals that died following acute studies revealed damage to the vascular system; congestion and haemorrhage of the lungs; and congestion or degeneration of the liver, kidneys, spleen, pancreas and intestines • Rats and rabbits exposed at 538 ppm for 4 h/d for 6 mo; disruption of hepatic function as shown by a decrease in hepatic glycogen and fat levels as well as prolonged hexenal sleep • Detected in the exhaled air of rabbits after 20 min of skin contact (no further information); shown to be absorbed through intact rabbit skin • 2 yr inhalation study in rats and mice; 0, 100, 200 or 400 ppm for 6 h/d, 5 d/wk for 2 yr: <ul style="list-style-type: none"> ○ 100 ppm and 200 ppm, no significant incidence of adverse effects ○ 400 ppm; an increased incidence of conjunctivitis in exposed female rats and in mice, increased pulmonary inflammation in the females and decreased body weight in males and females as compared to controls ○ 400 ppm increased incidence of nasal and alveolar epithelial hyperplasia ○ female mice developed adenomas, adenocarcinomas and squamous cell carcinomas of the uterus; combined frequency of 56% at 400 ppm; combine frequency of 11% at 200 ppm; combined frequency of 8% at 100 ppm; and 0% for controls ○ metastasised neoplasms in other organs likely responsible for decreased survival in female mice exposed at 400 ppm ○ male rats: increased production of pheochromocytomas of the adrenal medulla and granular cell neoplasms of the brain at 100 ppm; pulmonary adenomas and carcinomas at 200 ppm; not dose-related and not statistical significant from controls ○ female rats exposed at 400 ppm: marginal, nonsignificant increase in granular cell tumours of the brain and adenomas of the lung. 		



Source	Year set	Standard
<p>Positive mutagenicity in <i>S. typhimurium</i> strains TA1535, TA102 and TA100, negative in TA98; no further information</p> <p>In other tests; negative for mutagenicity in <i>S. typhimurium</i> in the standard non-enclosed NTP assay with and without S9 activation; with enclosed system positive with and without S9 activation</p> <p>Positive mutagenicity in as tryptophan dependent <i>E. coli</i> strain WP2(hc-) mutants.</p>		
DFG	1996	Not assigned
<p>Summary of additional data:</p> <ul style="list-style-type: none"> • MAK not assigned due to carcinogenicity • Carcinogenicity studies in rats and mice demonstrate carcinogenic potential in animals; insufficient evidence to evaluate carcinogenicity in humans • Clearly mutagenic in the Ames test in the <i>S. typhimurium</i> strains TA100 and TA1535; not TA98 (as per ACGIH, 2018). 		
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2015	<ul style="list-style-type: none"> • Critical effect of systemic long-term carcinogenicity • Volunteers exposed at 6,500 ppm for 5 min developed mild eye irritation • Positive mutagenicity • No appropriate <i>in vivo</i> studies are available to determine the genotoxic potential of the chemical.
NTP	✓ 1989	<ul style="list-style-type: none"> • Evidence of carcinogenicity in female mice, with dose-related increases of rare uterine tumours (adenomas, adenocarcinomas or squamous cell carcinomas), reaching statistical significance at ≥ 200 ppm • Increased incidences of alveolar/bronchiolar carcinomas and combined adenomas or carcinomas were observed in male mice at ≥ 200 ppm.
US EPA	✓ 1988	<ul style="list-style-type: none"> • Inadequate human and animal data; not classifiable as to human carcinogenicity • Has shown genotoxicity.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? Insufficient data

Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	Carc. 2, Skin
HCIS	Carcinogenicity – category 2
NICNAS	Carc. Cat 3
EU Annex	NA
ECHA	Carc. 2
ACGIH	Skin, Carcinogenicity – A3
DFG	H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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

Calculation	
Adverse effects in human case study:	yes
Dermal LD ₅₀ ≤ 1000 mg/kg:	
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	
<i>In vivo</i> dermal absorption rate > 10%:	
Estimated dermal exposure at WES > 10%:	
a skin notation is warranted	

IDLH

Is there a suitable IDLH value available? No, the chemical is a genotoxic carcinogen

Additional information

Molecular weight:	108.97
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.46 mg/m ³ ; 1 mg/m ³ = 0.224 ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> 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.

Deutsche Forschungsgemeinschaft (DFG) (1992) Ethyl bromide – MAK value documentation.

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

International Agency for Research on Cancer (IARC) (1999) Bromoethane. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2015) Ethane, bromo: Human health tier II assessment – IMAP report.

National Toxicology Program (NTP) 1989. Toxicology and Carcinogenesis Studies of Bromoethane (CAS No. 74-96-4) in F344/N Rats and B6C3F1 Mice (Inhalation Studies)

US Environmental Protection Agency (US EPA) (1998) Bromoethane IRIS Chemical Assessment Summary.