# ETHYLENE

**CAS number:** 74-85-1

**Synonyms:** Acetene, bicarburetted hydrogen, elayl, ethene, olefiant gas

**Chemical formula:** $C_2H_4$

## Workplace exposure standard (interim)

**TWA:** —

**STEL:** —

**Peak limitation:** —

**Notations:** —

**IDLH:** —

Sampling and analysis: **N/A**

## Recommendation and basis for workplace exposure standard

Insufficient data are available to perform a risk-based assessment. Therefore, it is recommended that an investigation of additional data sources be undertaken at the next scheduled review.

## Discussion and conclusions

Ethylene is a gas under standard conditions and is used as a starting material in the manufacture of plastics and small organic compounds, as a plant maturation hormone in the food industry and occasionally as an anaesthetic.

It is relatively non-toxic and causes anaesthesia and asphyxiation at extremely high concentrations (greater than 50,000 ppm). Approximately 0.5 to 4% is absorbed by inhalation and partly metabolised to ethylene oxide (EtO), which is a known genotoxic carcinogen (ACGIH, 2018; DFG, 1998; OECD, 1996). Modelled ADME data indicate that an external ethylene air concentration of 1,000 ppm equates to an internal exposure to EtO of 5.6 ppm in rats (ACGIH, 2018; DFG, 1998). External exposure to 5.6 ppm EtO is tumorigenic in rats (ACGIH, 2018). An air concentration of ethylene that yields such an internal EtO exposure however, showed no comparable carcinogenic or mutagenic activity in extensive animal studies or human case studies (ACGIH, 2018; DFG, 1998). Similarly, an ethylene air concentration of 45 ppm equates to an internal EtO exposure of 1 ppm, which demonstrated an increased incidence of leukaemia in workers (DFG, 1998). Systemic dermal toxicity or sensitisation effects are considered unlikely (ACGIH, 2018), but not discussed in the available source material.

A TWA for EtO (0.015 ppb) is proposed and is intended to minimise excess incidence of lung cancer in exposed workers. However, no ADME data are available to infer an equivalent ethylene exposure that yields an internal EtO concentration at this TWA. In the absence of a previous TWA recommendation and inconsistencies in the current database regarding potential genotoxic carcinogenicity (DFG, 1998), a TWA for ethylene is withheld in the interim. A detailed examination of the available data should be prioritised during subsequent reviews.

## Recommendation for notations

Not classified as a 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.

There are insufficient date to recommend a skin notation.

# APPENDIX

## Primary sources with reports

| Source | Year set | Standard |
|---|---|---|
| ***SWA*** | ***NA*** | ***NA*** |
| No report | | |
| ***ACGIH*** | ***2005*** | ***TLV-TWA: 200 ppm (230 mg/m$^3$)*** |

TLV-TWA intended to protect for asphyxiation.

Summary of data:

Considered to be non-toxic anaesthetic that causes asphyxiation by oxygen displacement. Observed liver toxicity in rats pre-treated with Aroclor 1254 considered irrelevant to workplace exposure.

TLV-TWA based on a NOAEL of 3,000 ppm from a chronic inhalational study with rats to which a UF of 15 is applied (derivation of UF not discussed).

Several experimental and modelled data show the substance is poorly bioavailable, but can be metabolised to EtO, a known carcinogen.

Human data:

- 2% of inhaled ethylene is metabolised in volunteer chamber study at 5–50 ppm (n=6, 2 h)
  - rate of metabolism is 3 times greater in rats
- Internal exposure to EtO at 45 ppm ethylene ≡1 ppm atmospheric EtO
  - ADME model agrees well with experimental data
- Case study of fruit store workers exposed at 0.3 ppm showed 3% of absorbed ethylene converted to EtO
  - exposed workers had ≈2 times more haemoglobin-ethylene adduct concentrations than unexposed workers
- Case study of workers in plastics industry exposed at 3.5–3.8 ppm showed that inhaled ethylene converted to EtO at a rate of 0.5%
- Increased risks (not specified) associated with exposures to mixtures of chemicals, including ethylene, in petrochemical workers
  - health risks not shown to increase with exposure/employment duration.

Animal data:

- Modelled ADME data generally agree well with experimental data:
  - inhalational absorption rate of 17% (rats); of the systemically available ethylene, 76% is exhaled unchanged
  - rats inhaling 1,000 ppm (160 min), exhaled EtO at peak of 0.6 ppm (45 min)
  - metabolism, including formation of haemoglobin and DNA adducts, reaches saturation at ≈1,000 ppm in rats and mice
  - assuming 100% conversion to EtO, internal exposure to EtO at 1,000 ppm ethylene ≡5.6 ppm air concentration of EtO (rats); 37 ppm ethylene ≡1 ppm atmospheric EtO (rats)
  - EtO exposure at 5.6 ppm is demonstrably tumorigenic in rats
  - predicted increase in tumour incidence due to internal EtO exposure at 1,000 ppm ethylene is 2% (rats), but not affirmed by chronic inhalation studies
- No adverse changes to heart, lungs, adrenals and kidneys after repeated anaesthetisation (mice, no further information)

| Source | Year set | Standard |
|---|---|---|
| • No adverse effects to liver at 50,000 ppm (rats, 4 h); only rats pre-treated with Aroclor showed increasing liver damage from 10,000–50,000 ppm<br>• No adverse effects in sub-chronic or chronic inhalational study, treatment range: 300–10,000 ppm (rats, 6 h/d, 5 d/wk, 2 wk or 2 yr)<br>• No effects on development or reproduction at 5,000 ppm (rats)<br>• Non-mutagenic *in vitro* and *in vivo*; concentration required to produce mutagenic level of EtO *in vivo* not achieved under experimental conditions.<br><br>No evidence to suggest a skin or sensitisation notation are necessary. Carcinogenicity studies in animals were negative, which supports an A4 classification. Insufficient data to recommend a STEL. | | |
| ***DFG*** | ***1998*** | ***Not assigned*** |
| Summary of additional data:<br>No MAK established based on potential carcinogenicity of EtO metabolite. Available animal carcinogenicity data may be inadequate to demonstrate low level of carcinogenicity. No positive results available from epidemiological or carcinogenicity studies; therefore, assigned in carcinogenicity group 3B. Notes that several epidemiological studies of EtO exposure equivocally indicate an association with increased cancer risk.<br>Skin absorption and sensitisation effects not presented.<br>Human data:<br>• No reports of acute exposure<br>• Rate of ethylene metabolism is directly related to exposure concentration up to 50 ppm in humans (cf. 80 ppm in rats)<br>• From internal exposure to endogenous ethylene, average concentration of EtO is 0.17 nmol/kg; occupational exposure to 45 ppm ethylene (assuming 8 h/d, 5 d/wk, 52 wk/yr, 45 yr) ≡14 nmol/kg EtO, which would also be reached at an EtO exposure of 1 ppm over the same period:<br>o calculation used in risk assessment to address indistinguishability of tumorigenicity between exposure and control groups in chronic animal studies<br>• Evidence for genotoxicity in workers occupationally exposed to EtO at 0.025 ppm<br>• 2 epidemiological studies indicate increased risk of leukaemia at exposures 20±10 ppm for 4–10 yr (n=70); calculated risks at 1 ppm for occupational exposure (assuming 8 h/d, 5 d/wk, 46 wk/yr, 45 yr) =1.2–6.4% and life-time exposure risk =50%.<br>Animal data:<br>• The rate of metabolism of ethylene is possibly too low to result in sufficient EtO concentrations that increase tumorigenicity above control groups in standard carcinogenicity studies. | | |
| ***SCOEL*** | ***NA*** | ***NA*** |
| No report. | | |
| ***OARS/AIHA*** | ***NA*** | ***NA*** |
| No report. | | |

| Source | Year set | Standard |
|---|---|---|
| ***HCOTN*** | ***NA*** | ***NA*** |

Summary of additional data:

- Amount of EtO formed from ethylene metabolism is insufficient to elicit carcinogenic effects under reported conditions
- 2 available epidemiological studies of exposed workers are unreliable due to mixed exposures to other known carcinogens
- Insufficient data to evaluate carcinogenicity of the substance.

### Secondary source reports relied upon

| Source | | Year | Additional information |
|---|---|---|---|
| IARC | ✓ | 1994 | • Inadequate evidence for carcinogenicity experimental animals and humans; not classifiable as to its carcinogenicity to humans. |
| OECD | ✓ | 1996 | • 2 part study of Swedish petrochemical plant reported elevated and dose-related levels of the EtO haemoglobin adduct in workers exposed to 0.35 and 3.5 ppm compared to control group exposed to 0.001 ppm:<br>o results indicated that 1–4% of the inhaled ethylene was metabolised to ethylene oxide. |

### 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 | NA |
| HCIS | — |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4 |
| DFG | Carcinogenicity – 3B |
| SCOEL | NA |
| HCOTN | Carcinogenicity – category 3 |

| Source | Notations |
|---|---|
| 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 |
|---|
| Insufficient data to assign a skin notation. |

### IDLH

Is there a suitable IDLH value available? No

## Additional information

| | |
|---|---|
| Molecular weight: | 28.05 |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 1.15 mg/m$^3$; 1 mg/m$^3$ = 0.87 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.

Deutsche Forschungsgemeinschaft (DFG) (1998) Ethylene – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2013) Ethylene. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2013/24.

International Agency for Research on Cancer (IARC) (1994) Ethylene. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 71.

Organisation for Economic Cooperation and Development (OECD) (1996) SIDS initial assessment profile – Ethylene.