# Ethyl formate

| CAS number: | 109-94-4 |
| --- | --- |
| Synonyms: | Ethyl methanoate, formic acid ethyl ester |
| Chemical formula: | C3H6O2 |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **100 ppm (303 mg/m3)** |
| --- | --- |
| STEL: | **150 ppm (462 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **1,500 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 100 ppm (303 mg/m3) is recommended to protect for eye and upper respiratory tract irritation in exposed workers.

A STEL of 150 ppm (462 mg/m3) is recommended to protect for acute eye and upper respiratory tract irritation.

## Discussion and conclusions

Ethyl formate is used as a solvent, fungicide, larvicide, and flavouring agent. Critical effects are progressive irritation of the upper respiratory tract and eyes.

Slight eye and upper respiratory tract irritation are reported in humans exposed above 330 ppm (ACGIH, 2018; DFG, 2013). Data indicate that while these effects are reversible, they are progressive and may persist for up to four hours following exposure (DFG, 2013). Enzymatic hydrolysis produces acidic metabolites, which are rapidly eliminated and not expected to accumulate from exposure below 100 ppm (DFG, 2013; HCOTN, 2002). The current TWA of 100 ppm is recommended to be retained and is same as the recommendations by DFG and HCOTN. This TWA is expected to be protective of irritation effects in humans (ACGIH, 2018; DFG, 2013, HCOTN, 2002).

Exposures at 1,000 ppm are associated with strong pungency and nuisance (ACGIH, 2018). Therefore, a STEL of 150 ppm adopted from HSE (2002) is considered protective of these effects, given their progressive nature.

## 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.

A skin notation is not warranted based on the available evidence. ACGIH has not assigned a skin notation due to limited evidence for appreciable dermal absorption and subsequent systemic toxicity in animals or humans (ACGIH, 2018). The DFG (2013) assigns a skin notation by analogy to the structurally related methyl formate, which is inconsistent with other primary sources.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 100 ppm (303 mg/m3) | |
|  |
| ACGIH 2012 TLV-STEL: 100 ppm (303 mg/m3) |
| TLV-STEL intended to protect for irritation of the upper respiratory tract and CNS effects.  Summary of data:  TLV-STEL derived from human sensory data that shows respiratory and eye irritation above 330 ppm, which is supported by signs of irritation in animals at 5,000 ppm. Assigning a TLV-STEL instead of a TLV-TWA not discussed, but previous value of 100 ppm was withdrawn in 2012. No chronic inhalational data reported.  Human data:   * Odour threshold: 30 ppm; nasal stimulation threshold: 18,800 ppm (n=72) * Upper respiratory irritation at 330–1,000 ppm (no further details provided) * Weakly pungent at 100 ppm; strongly pungent and annoying at 1,000 ppm (n=48) * Slight eye irritation at 330 ppm and increasing nasal irritation (no further information); progressive and persistent eye and mucous membrane irritation at 10,560 ppm * Non-sensitising in patch test at 4% in petrolatum (n=23).   Animal data:   * Oral LD50: 1,800–4,290 mg/kg (rats), 2,100 mg/kg (rabbits); median narcotic dose also 2,100 mg/kg (rabbits) * LD50: >18,300 mg/kg (rabbits, dermal); no- or low dermal irritation noted * Readily hydrolysed upon absorption to formic acid and ethanol, which can pass through alveoli and gastrointestinal wall * Fatal by inhalation at 8,000 ppm (rats, 4 h) and 10,000 ppm (cats, 90 min), eye irritation and salivation at 5,000 ppm (20 min), narcosis and pulmonary oedema at 10,000 ppm (80 min) * No histopathological or haematological changes when administered in diet at 100–1,000 mg/kg/d (young rats, 17 wk); no evidence for carcinogenicity * No higher incidence of lung tumours when maximally tolerated dose (MTD) or 20% of MTD was administered intraperitoneally (mice, 24 injections, 8 wk) * Non-mutagenic *in vitro*, but increases lethal mutations in *Drosophila* eggs.   Several long-term exposure studies indicate ethyl formate is not classifiable as a human carcinogen. Insufficient data to recommend notations for skin absorption or sensitisation. |
| DFG 2013 MAK: 100 ppm (310 mg/m3) |
| Summary of additional data:  Accumulation and acidosis from acidic metabolites not expected to occur <100 ppm. Assuming a 70 kg worker with a respiratory volume of 10 m3 during an 8 h shift and 100% absorption, exposure of 100 ppm ≡5.4 mg/kg/h, which is significantly lower than relevant elimination rates of either metabolite, formic acid (34 mg/kg/h) and ethanol (85–100 mg/kg/h). MAK therefore retained.  Human data:   * Slight eye irritation and rapidly progressing nasal irritation at 330 ppm persisted for 4 h following exposure (duration not specified).   Animal data:   * 17 wk feeding study (also reported by ACGIH) considered unsuitable due to volatility of the substance.   No peak limitation derived due to absence of NOAEL for irritation. Toxic effects on reproduction reported *in vitro* not expected if MAK is observed. Skin notation is recommended by analogy to structurally related methyl formate. Insufficient data to recommend a sensitiser notation. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2002 8-hour TWA: 100 ppm (300 mg/m3) |
| Summary of additional data:  Available toxicological database considered insufficient to make health-based recommendation on current administrative OEL. However, no accumulation of the substance or its metabolites is expected if the current OEL is observed and protective for systemic adverse effects.  Animal data:   * Inhalation of saturated vapour caused mortality after 5 min (rats, guinea pigs); tremors and death occurred from circulatory and respiratory failure (guinea pigs) * CNS depression and pneumonia at 12,800–41,600 ppm (rabbits, guinea pigs, >1 min); * Pulmonary oedema at 10,000 ppm (dogs, 4 h) * Severe burns when 0.02 mL of undiluted ethyl formate applied to rabbit eyes * Repeat intraperitoneal injection study (also reported by ACGIH) showed no higher incidence of lung tumours at total doses of 2,400–12,000 mg/kg (mice, 24 injections, 8 wk), but considered insufficiently documented to draw conclusion on carcinogenicity * No genotoxicity data available for *in vivo* or *in vitro* mammalian test systems. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| HSE |  | 2002 | * TWA: 100 ppm (308 mg/m3) * STEL: 150 ppm (462 mg/m3). |
| NTP |  | 2018 | * Negative Ames test. |
| US NIOSH |  | 1994 | * IDLH based on acute inhalation toxicity data in animals; conservative value due to lack of relevant acute toxicity data for workers at concentrations >330 ppm. |

### 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 | — |
| HCIS | — |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | — |
| ACGIH | Carcinogenicity – A4 |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | — |
| IARC | NA |
| 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: | no |  |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  |  | **a skin notation is not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 74.08 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 3.03 mg/m3; 1 mg/m3 = 0.330 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*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2003) Formic acid ethyl ester – MAK value documentation.

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

Health Council of the Netherlands (HCOTN) (2002) Ethyl formate. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/033.

National Toxicology Program (NTP) (2018) Toxicity Evaluation of Ethyl Formate in Salmonella/E.coli Mutagenicity Test or Ames Test: Study A02552.

UK Health and Safety Executive (HSE) (2002) EH40/2005 Workplace exposure limits.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Ethyl formate.