# Ethyl alcohol

| CAS number: | 64-17-5 |
| --- | --- |
| Synonyms: | Ethanol, absolute ethanol, anhydrous ethanol, alcohol, denatured alcohol, methyl carbinol, synasol |
| Chemical formula: | C2H6O |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **200 ppm (380 mg/m3)** |
| --- | --- |
| STEL: | **800 ppm (1,500 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **3,300 ppm (LEL)** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 200 ppm (380 mg/m3) is recommended to protect for central nervous system effects, carcinogenicity and liver effects in chronically exposed workers.

A STEL of 800 ppm (1,500 mg/m3) is recommended to protect for transient irritation from acute exposures.

## Discussion and conclusions

Ethyl alcohol encountered in the workplace is used as a solvent, additive to disinfectants or as a starting material in various chemical manufacture and pharmaceutical settings.

Adverse effects are transient eye irritation and depression of CNS after short exposure and after long-term exposure, potential hepatotoxicity, developmental effects and carcinogenicity. Carcinogenic and developmental effects resulting from the consumption of alcoholic beverages are discussed in most source material. However, these effects are only observed at extremely high levels of alcohol consumption and are unlikely to occur from inhalational or dermal exposure in the workplace (ACGIH, 2018; HCOTN, 2005, NICNAS, 2014). Local irritation is demonstrated at concentrations between 1,000 and 1,900 ppm in volunteers, which is the basis of the ACGIH TLV-STEL (2018). Translation of oral toxicity in humans to an inhalational equivalent suggests an occupational exposure of 690 to 790 ppm would not increase the risk of cancer appreciably above the existing risk associated with internal exposure to endogenous ethyl alcohol (DFG, 2017; HCOTN, 2005). On this basis, the HCOTN (2005) recommends a 15 minute STEL of 1,000 ppm, whereas the DFG (2017) has amended the previous MAK of 500 ppm to 200 ppm to account for a two to three-fold increased body burden resulting from higher bioavailability under exertion as demonstrated in a volunteer study.

It is recommended that the TWA is amended in alignment with the approach presented by the DFG (2017) as it is anticipated to be protective of effects on the CNS and liver. This value will also be protective of any potential carcinogenic associated with long-term exposure. A STEL of 800 ppm is also recommended and expected to be protective of transient irritation effects resulting from acute exposures and is supported by the evaluations of the ACGIH (2018) and HCOTN (2005).

## 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 recommended as there is no indication of systemic effects resulting from skin absorption at exposures relevant to the workplace.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 1,000 ppm (1,880 mg/m3) | |
|  |
| ACGIH 2009 TLV-STEL: 1,000 ppm (1,880 mg/m3) |
| TLV-STEL intended to protect for irritation to eyes and upper respiratory tract.  Chronic exposure leads to liver cirrhosis and adverse developmental and fertility effects in animals.  A TLV-TWA is not recommended as the TLV-STEL is expected to be protective of both acute irritational and chronic systemic effects.  Confirmed animal carcinogen with unknown relevance to humans. Carcinogenic classification of alcoholic beverages considered irrelevant to workplace exposure.  Summary of data:  TLV-STEL based on weight of evidence from volunteer studies that generally showed no irritation effects at 1,000 ppm.  No excess cancer risk expected from workplace exposure, excessive alcohol consumption may elevate this risk if internal exposures are compounded.  Human data:   * No evidence for developmental toxicity at workplace exposure levels * Lung absorption rate: 62%, assuming a respiratory volume of 10 m3 during an 8 h shift effective dose at 1,000 ppm ≡12 g ≈1 standard alcoholic beverage * No accumulation in tissue expected at 1,000 ppm due to rapid clearance and metabolism * Transient coughing and stinging in eyes at 5,000–10,000 ppm in volunteer inhalation study;   + symptoms subsided after 5–10 min   + continuous lachrymation and coughing at 15,000 ppm (durations not specified) * No adverse effects at 80–1,000 ppm in volunteer inhalation study (n=12/sex, 4 h);   + increasing-dose experiment of same study showed 100–1,900 ppm (average: 1,000 ppm) to be a nuisance * Dermal sensitisation in 6/93 volunteers to 50% aqueous solution; 2 had allergic reactions * No epidemiological studies with vapour, but alcoholic beverages shown to cause cancer of the mouth, oesophagus and liver and liver cirrhosis.   Animal data:   * LC50: 13,000 ppm (rats, 22 h); 22,000 ppm (guinea pigs, 9 h); 29,000 ppm (mice, 7 h)   + signs of intoxication are ataxia, incoordination, drowsiness; narcotic dose: 20,000 ppm (rats, 2 h) * Median respiratory depression (RD50): 13,000–27,000 ppm (mice); sensory irritant * LD50: 6,200–17,800 mg/kg (various unspecified species, oral) * *In vitro* dermal absorption ≈1% (guinea pig skin, 19 h) * No histological or haematological toxicity in continuous inhalation studies at 46 ppm (rats, guinea pigs, rabbits, monkey, dogs, 90 d)   + separate inhalation study also reported no adverse effects at 3,000 ppm (guinea pigs, 4 h/d, 6 d/wk, 10.5 wk) * No changes to fertility at 10,000–16,000 ppm (male rats, 7 h/d, 6 wk) * Rate of resorptions increased but no foetal malformations at 7,950 ppm continuous exposure (mice, GD 7–9 or 7–12);   + congenital malformations in inhalational study at 20,000 ppm (rats, 7 h/d, GD 1–19), NOAEL: 10,000 ppm * Generally non-genotoxic *in vivo*, but can induce SCE (no further information)   + genotoxic *in vitro* if test system can metabolise ethanol. |
| DFG 2017 MAK: 200 ppm (380 mg/m3) |
| Summary of additional data:  CNS effects and long-term carcinogenicity considered as critical effects.  MAK derived from lifetime body burden calculation to minimise potential for excess carcinogenicity above endogenous baseline levels. Exposure at 790 ppm during an 8 h shift with a respiratory volume of 10 m3 and 62% lung absorption results in blood ethanol levels within a standard deviation of the endogenous baseline concentrations. The previous MAK of 500 ppm was therefore preventative of potential carcinogenic effects and irritation effects observed above 1,000 ppm in volunteer studies (also cited by ACGIH, 2018).  The current MAK is derived similarly by dividing the previous value by 2.5 regarding additional data that indicate body burden rises 2–3-fold during exercise.  Skin notation not warranted based on derivation using previous MAK value.  Human data:   * Odour threshold: 80 ppm, eye irritation threshold: 80,000 ppm * Body burden shown to be 2–3 times higher during exercise than at rest in volunteer chamber study 125, 250, 500, 750 and 1,000 ppm at rest or 750 ppm during exercise (n=5/sex, 4 h)   + blood ethanol concentrations return to baseline within 1 h after cessation * Lifetime body burden due to endogenous ethanol calculated to be 0.27±0.17 mg/L in blood   + following equilibration, exposures at air concentrations up to 790 ppm do not raise blood concentrations higher than 1 standard deviation from endogenous levels assuming 8 h/d, 5 d/wk for 40 yr * Skin permeability: 3.2 µm/h ≡0.25 mg/cm2/h, exposure of 2,000 cm2 skin to pure ethanol for 1 h delivers an effective dose of 500 mg   + at the current MAK, an effective inhalational dose of ≈2,280 mg would be delivered in an 8 h shift.   Animal data:   * Mortality after dermal application of 20,000 mg/kg (rabbits) * *In vivo* genotoxicity (increased SCE) at highly toxic doses (mice, 8,000 mg/kg ip injection, cumulative dose over GD 16–18). |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2006 15-min STEL: 1,000 ppm (1,900 mg/m3) |
| Summary of additional data:  Extensive review of oral route data for humans and animals due to limited inhalational studies. Oral route studies are considered relevant as acetaldehyde is generated as a primary metabolite, which has genotoxic properties.  Considers the substance to be a non-threshold genotoxic carcinogen based on the available oral intake studies. However, cited studies indicate genotoxic effects are only observed at extremely high concentrations *in vivo*, which are unlikely to occur from inhalational or dermal exposure in the workplace. An occupational exposure at a level that would minimise an excess risk of breast cancer risk to 4x10-5 results in an additional ethanol body burden (0.2 mg/L/yr), which is significantly lower than that produced by internal exposure to endogenous ethanol (22 mg/L/yr).  A health-based calculated occupational cancer risk value (HBC-OCRV) of 690 ppm (1,300 mg/m3), corresponding to a breast cancer risk in women of 4x10-3 for 40 yr of occupational exposure and a 15 min STEL of 1,000 ppm (1,900 mg/m3) are recommended.  Despite current administrative standard, skin notation not warranted due to low dermal uptake relative to the recommended HBC-OCRV.  Human data:   * Positive association between alcohol intake and breast, throat and liver cancers   + no evidence for a threshold value below which no cancer risk exists * DECOS evaluate that oral intake of 10,000 mg expected to increase risk of breast cancer by 7–10%, which corresponds to a risk ratio (RR) of 1.1 and yields the exposure-response relationship:   + Background rate of breast cancer deaths in Netherlands is 12.5 per 250 deaths/yr   + Excess lifetime cancer risk of +1 death/yr due to breast cancer corresponds to or an additional risk of 4x10-3at an exposure to 8,000 mg/d   + An air concentration that delivers an effective oral dose of 8,000 mg/d is 690 ppm (1,300 mg/m3) assuming 60% inhalational absorption and a respiratory volume of 10 m3 ­­during an 8-h shift   + An air concentration with an associated additional risk of 4x10-5 is assumed to be 7 ppm (13 mg/m3) ≡0.2 mg/L/yr ethanol body burden from occupational exposure, which is lower than that of lifetime body burden caused by endogenous ethanol (22 mg/L/yr) and considered negligible by the agency   + DECOS therefore recommend an HBC-ORCV of 690 ppm (1,300 mg/m3), which would result in a blood alcohol content that is 1–100 times lower than that required to produce reproductive and developmental toxicity   Animal data:   * Non-mutagenic in most *in vitro* assays, metabolic activation generally required for positive results. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| HSE |  | 2002 | TWA: 1,000 ppm (1,920 mg/m3) |
| NICNAS |  | 2014 | * Overall, the data indicates no mutagenic or genotoxic potential * Use in alcoholic beverages not considered for workplace assessment, evaluation of carcinogenicity of alcoholic beverages may not be relevant to occupational exposure or use in consumer products * Available animal studies mostly report oral exposure, which exceed MTD and may be irrelevant to occupational exposure; carcinogenicity classification therefore considered inappropriate * *In* vivo genotoxicity assays are equivocal; confounded by inadequate methodologies and use of high doses.   + the most robust dominant lethal testing was of male mice exposed by intubation below the maximally tolerated dose: no significant effects reported * Exposure through consuming alcoholic beverages is associated with increased risk of carcinogenicity and reproductive/developmental toxicity, which increase in a dose-dependent manner, but are not considered relevant at levels relating to occupational exposure * critical health effect for risk characterisation from industrial use is therefore local eye irritation. |
| IARC |  | 2012 | Conclusions of evaluation pertain to the consumption of alcoholic beverages and carcinogenicity of primary metabolite, acetaldehyde   * Sufficient evidence in humans for the carcinogenicity of acetaldehyde associated with the consumption of alcoholic beverages * Acetaldehyde associated with the consumption of alcoholic beverages causes cancers of the oesophagus and of upper aerodigestive tract Sufficient evidence in experimental animals for the carcinogenicity of ethyl alcohol and acetaldehyde * Alcohol consumption is carcinogenic to humans; ethyl alcohol in alcoholic beverages is carcinogenic to humans (Group 1) * Sufficient epidemiological evidence shows that humans deficient in the oxidation of acetaldehyde to acetate have increased risk for developing alcohol-related cancers, e.g. in the oesophagus and the upper aerodigestive tract. |
| US NIOSH |  | 1994 | IDLH based 10% of the lower explosive limit. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | No |
| --- | --- |
| **The chemical is not a non-threshold based genotoxic carcinogen.** | |

## Notations

| Source | Notations |
| --- | --- |
| SWA | — |
| HCIS | — |
| NICNAS | — |
| EU Annex | — |
| ECHA | NA |
| ACGIH | Carcinogenicity – A3 |
| DFG | NA |
| SCOEL | NA |
| HCOTN | Skin |
| IARC | Carcinogenicity – Group 1 (*alcoholic beverages*) |
| 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: |  |  |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: | no | -3.00 |  | | Estimated dermal exposure at WES >10%: | yes | 2.00 |  | |  |  | -0.5 | **a skin notation is not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes, based on LEL |
| --- | --- |

## Additional information

| Molecular weight: | 46.07 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 1.88 mg/m3; 1 mg/m3 = 0.532 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) (2017) Ethanol – MAK value documentation, German language edition.

Health Council of the Netherlands (HCOTN) (2006) ethanol. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2006/06OSH.

International Agency for Research on Cancer (IARC) (2012) Personal Habits and Indoor Combustions. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 100E.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Ethanol: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

UK Health and Safety Executive (HSE) (1992) ethyl alcohol – EH64: Summary criteria for occupational exposure limits.

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