# Vinyl acetate

| CAS number: | 108-05-4 |
| --- | --- |
| Synonyms: | Acetic acid vinyl ester, vinyl A monomer, 1-acetoxyethylene, ethenyl acetate, ethynyl ethanoate, ethanoic acid ethenyl ester, vinyl ethanoate |
| Chemical formula: | C4H6O6 |

 Workplace exposure standard (amended)

| TWA: | **10 ppm (35 mg/m3)** |
| --- | --- |
| STEL: | **15 ppm (53 mg/m3)** |
| Peak limitation: | **—** |
|  Notations: | **Carc. 2** |
| 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 10 ppm (35 mg/m3) is recommended to protect for irritant effects and carcinogenicity in exposed workers.

A STEL of 15 ppm (53 mg/m3) is recommended to protect for acute irritant effects in exposed workers.

## Discussion and conclusions

Vinyl acetate is used as an emulsifier in polymer, ink, adhesive, paint, textile and paper production.

The critical effects of exposure are irritation of the upper respiratory tract and carcinogenicity.

Thresholds for local irritation vary in the available human exposure data. A single exposure at 4 ppm for two minutes or 20 ppm for four hours is irritating to some volunteers and a 30-minute exposure at 72 ppm is irritating to all volunteers. These data are generally consistent with the results of a workplace study that associates respiratory irritation with air concentrations of 21.6 ppm and above; with no adverse effects reported at 5 to 10 ppm (ACGIH, 2018). Available epidemiological data are indicative of carcinogenicity but limited by confounding co-exposures and small case numbers (ACGIH, 2018; DFG, 2005). Carcinogenicity is reported in chronically exposed rodents *via* inhalation at 600 ppm or oral routes at 1,000 ppm in drinking water (ACGIH, 2018; DFG, 2005). The dose‑response relationship for tumorigenicity is non-linear and suggests a threshold for carcinogenic effects, which depends on the action of chronic irritation and saturation of acetaldehyde-forming metabolic pathways (ACGIH, 2018; DFG, 2005). A NOAEC of 50 ppm for histopathological signs of irritation is reported in a chronic inhalation study with mice and rats (ACGIH, 2018; DFG, 2005).

DFG (2005) considers the available human irritation and carcinogenicity data insufficient for the basis of an OEL recommendation. The evaluations of ACGIH (2018) and SCOEL (2005) use the NOAEC of 50 ppm for upper respiratory irritation in rodents as a point of departure. The TWA of 10 ppm and STEL of 15 ppm are supported by limited human exposure data that suggest irritation occurs near 20 ppm over prolonged exposure, but not at 10 ppm. In view of this information, the TWA of 10 ppm and STEL of 15 ppm are recommended and expected to protect for local irritation and potential carcinogenicity.

## 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 not recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard  |
| --- |
| SWA 1991 TWA: 10 ppm (35 mg/m3); STEL: 20 ppm (70 mg/m3) |
|  |
| ACGIH 2018 TLV-TWA: 10 ppm (35 mg/m3); TLV-STEL: 15 ppm (53 mg/m3) |
| TLV-TWA and TLV-STEL intended to protect for respiratory tract irritation. Summary of information:TLV-TWA based on NOAEC of 50 ppm for microscopic changes indicative of URT irritation in rats and mice in chronic inhalation studies. TLV-STEL based on separate reports of eye and URT irritation in humans exposed at 21.6 and 72 ppm.Human data:* No differences in haematological parameters between controls and workers exposed on average at 5–10 ppm (peaks 300 ppm); irritation of eyes and throat reported in workers exposed at 21.6 ppm
* No irritation to eyes and throat at 1.3 ppm (2 min). Throat irritation at 4 ppm (2 min) in 1/9 volunteers and at 72 ppm (30 min) in 9/9 volunteers; irritation at 20 ppm (4 h) in 1/3 volunteers
* Excess risk of respiratory system and CNS cancers in epidemiological study of exposed workers (n=4,806); confounded by co-exposures to other chemicals including vinyl chloride, chlorinated solvents and acrylonitrile; subgroup of cases with slightly higher cumulative exposure to vinyl acetate associated with lung cancer
* Increased OR for incidence of NHL in 7/52 males (OR=1.2), multiple myeloma in 3/20 males (OR=1.6), lymphocytic leukaemia in 2/18 males (OR=1.8) in case-control study of exposed workers in 3 workplaces (n=29,139):
* ACGIH considers results inconclusive due to small numbers of cases and workers
* No positive patch test reactions to 1% solution of exposed workers (n=76).

Animal data:* Oral LD50: 2,920–3,470 mg/kg (rats), 1,613 mg/kg (mice)
* NOAEC: 36 ppm for decreased excitability of CNS reported in acute inhalation study (rabbits, 40 min):
* LOAEC of 71 ppm
* higher excitability at 142 ppm
* No change in liver enzyme levels and liver pathology at 250 mg/kg as single IP injection (guinea pigs):
* mortality and marginally increased liver enzyme activity at 500 mg/kg
* Decreased body weight, respiratory distress, increased lung/body ratio and inflammatory histological changes in the respiratory tract at 1,000 ppm (rats) and 200 ppm (mice) reported in subchronic inhalation study (6 h/d, 5 d/wk, 90 d)
* No changes in haematology, blood chemistry, organ weights or histopathology at 200‑5,000 ppm of drinking water in subchronic oral dose study (rats, 13 wk):
* growth rate reduced non-significantly at 5,000 ppm of drinking water (males only)
* NOAEL of 50 ppm for microscopic evidence of respiratory tract irritation and reduced body weight in chronic inhalation study at 0, 50, 200 and 600 ppm (mice, rats, 2 yr, no details on exposure duration and frequency):
* tumours in nasal cavity (rats) and lungs (mice) at 600 ppm
* tumours in rats considered to be due to chronic irritation
* Increased incidence of tumours in oesophagus and forestomach (females and their offspring) at 5,000 ppm in drinking water in chronic 2-gen oral dose study with exposure groups 0, 1,000 and 5,000 ppm (mice, 78 wk):
* 2 and 12% incidence of tumours of oral cavity and tongue at 1,000 and 5,000 ppm, respectively (0 in controls)
* 4 and 8% incidence of oesophagus and forestomach at 5,000 ppm in offspring of rats reported in the same study (rats, 104 wk); 2 and 6% oral cavity tumours at 1,000 and 5,000 ppm
* Cited review of several animal carcinogenicity data concludes substance is carcinogenic at site of entry
* Mutagenic *in vitro* in bacteria and mammalian cells in the presence or absence of metabolic activation; chromosomal aberrations detected in human whole-blood lymphocyte cultures
* DNA binding and induction of sister chromatid exchange at half the LD50
* Genotoxicity likely mediated by acetaldehyde metabolite.

Carcinogenicity confirmed in chronic feeding studies with animals but not confirmed in human epidemiological data (A3).Insufficient data to recommend notations for skin absorption or sensitisation. |
| DFG 2002 Not assigned |
| Summary of additional information:Previous MAK of 10 ppm withdrawn due to classification as non-genotoxic carcinogen. Insufficient data to assign a MAK at which potential carcinogenicity may not be expected (3A). Skin notation not recommended due to low dermal absorption potential regarding calculated NOAEC for systemic effects in humans and modelled dermal penetration data; starting from a NOAEC of 50 ppm (175 mg/m3) for systemic effects (measured as decreased body weight in mice, also presented in ACGIH, 2018), daily human equivalent oral intake ≈12,250 mg for a 70 kg worker.Human data:* 2 epidemiological studies (also presented in ACGIH, 2018) dismissed due to confounding co-exposures
* Modelled dermal intake from 2 reports: 541 mg and 68 mg assuming saturated aqueous solution on 2,000 cm2 skin over 1 h.

Animal data:* Positive skin sensitisation in non-guideline-compliant sensitisation test with undiluted substance (guinea pigs, 9 times in 3 wk for induction, provocation after 2 wk):
* DFG considers results of study confounded by irritative effect
* Positive carcinogenicity in chronic exposure studies with mice and rats (also reported in ACGIH, 2018) likely due to local metabolism to acetaldehyde and subsequent cytotoxicity and genotoxic effects of this metabolite:
	+ non-linear dose-response relationship regarding carcinogenicity inferred threshold for this effect, but not established in the current data set
* Not considered mutagenic based on negative results *in vivo* following inhalation or administration in drinking water (mice); micronucleus formation observed following high single IP dose (mice, also reported in ACGIH, 2018)
	+ metabolism to acetaldehyde contributes to endogenous acetaldehyde burden.

Insufficient data to recommend a sensitiser notation. |
| SCOEL 2005 TWA: 5 ppm (17.6 mg/m3); STEL: 10 ppm (35.2 mg/m3) |
| Summary of additional information:Animal carcinogenicity and mechanistic data indicate carcinogenesis caused by chronic irritation and consequent regenerative processes from acetaldehyde and acetic acid metabolites. Therefore, prevention of irritation should protect for carcinogenicity. STEL based on NOAEC of 50 ppm for microscopic lesions in nasal tissue of chronically exposed mice and rats (also reported in ACGIH, 2018 and DFG, 2005) and limited evidence for NOAEC of ≈10 ppm for irritation in humans (ACGIH, 2002 report cited without further details). TWA based on half the value of the STEL, both values expected to be sufficiently low to protect for irritation and potential carcinogenicity.Skin notation not recommended due to low dermal uptake relative to exposure at the OEL.* Not mutagenic based on negative results *in vivo* following inhalation or administration in drinking water (mice); micronucleus formation observed following high single IP dose (mice, also reported in ACGIH, 2018 and DFG, 2005).

Insufficient data to recommend a sensitiser notation. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | * LD50: 2,335–7,440 mg/kg (rabbits, dermal)
* Positive mutagenicity *in vitro* in mammalian cells; genotoxicity possibly attributable to formation of acetaldehyde or acidification from metabolism of large doses to acetic acid
* Mutagenic *in vivo*:
	+ increased frequency of chromosomal aberrations in cultured human lymphocytes from exposed workers (no further details provided)
	+ increased micronucleus formation at 1,000 and 2,000 mg/kg IP injection, but not at 750 mg/kg (mice)
	+ abnormal sperm at 500 mg/kg (mice); dose-dependent decrease in testicular weight from 125–500 mg/kg.
 |
| IARC |  | 1995 | * Eye and nose irritation thresholds reported at 10–22 ppm; throat irritation at 200 ppm and eye irritation at 72 ppm reported in separate study (both studies reported in ACGIH, 2018)
* Inadequate evidence for carcinogenicity in humans, limited evidence for carcinogenicity in animals; overall possibly carcinogenic to humans (Group 2B) supported by the following evidence:
	+ rapidly metabolised into acetaldehyde in human blood and animal tissues
	+ both vinyl acetate and acetaldehyde induce nasal cancer in rats following inhalation
	+ both vinyl acetate and acetaldehyde are genotoxic to human cells *in vitro* and animal cells *in vivo*.
 |
| ECHA |  | 2020 | * DNEL adopted from SCOEL (2005) recommendation in accordance with the agency’s evaluation and absence of additional information.
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### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| 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 | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat 3 |
| EU Annex | Carcinogenicity – category 2 |
| ECHA | Carc. 2 |
| ACGIH | Carcinogenicity – A3 |
| DFG | Carcinogenicity – 3A |
| SCOEL | — |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 2B |
| 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  |
| --- |
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| --- | --- | --- | --- |
| 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%: |   |   |   |
| Estimated dermal exposure at WES >10%: |   |   |   |
|   |   |   | **a skin notation is not warranted** |

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### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 86.09 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa:  | 1 ppm = 3.52 mg/m3; 1 mg/m3 = 0.28 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) (2005) Vinyl acetate – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2005) Recommendation from the Scientific Committee on Occupational Exposure Limits for Vinyl Acetate. SCOEL/SUM/122.

International Agency for Research on Cancer (IARC) (1995) Vinyl acetate. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Acetic acid, ethenyl ester: Human health tier II assessment – IMAP report.