# 1,3-Dioxolane

| CAS number: | 646-06-0 |
| --- | --- |
| Synonyms: | 1,3-Dioxacyclopentane, 1,3-Dioxolan, dioxolane, 1,3‑Dioxole, dihydroethylene glycol formal, glycolformal |
| Chemical formula: | C3H6O2 |
| Structural formula: | — |

Workplace exposure standard (new)

| TWA: | **20 ppm (61 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| 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 20 ppm (61 mg/m3) is recommended to protect for haematological (blood) disturbances and potential developmental effects in exposed workers.

## Discussion and conclusions

1,3-Dioxolane is used as in polymer and halothane production, and as a solvent.

Limited carcinogenicity and genotoxicity data indicate a low potential for mutagenic activity (ACGIH, 2018), with currently available *in vivo* studies contradictory (DFG, 2007). Available skin absorption data are conflicting, which indicate that despite low systemic toxicity in rabbits (ACGIH, 2018), modelled dermal flux rates account for significant contribution to overall exposure (DFG, 2007).

Critical effects are liver and spleen damage and reduced white blood cell (WBC) counts as reported in animal studies (ACGIH, 2018). Human exposure data is limited to a documented workplace study involving mixed exposures that reported no adverse haematological effects (ACGIH, 2018; DFG, 2018).

The recommended TWA is based on an inhalational NOAEC of 300 ppm for haematological changes in rats (ACGIH, 2018); a factor of 10 is applied and rounded down to derive a TWA of 20 ppm. This value is also expected to be protective of developmental effects reported in rats (DFG, 2018).

## 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 data to recommend a skin notation.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA NA NA | |
|  |
| ACGIH 2002 TLV-TWA: 20 ppm (61 mg/m3) |
| Summary of data:  TLV-TWA intended to minimise potential for systemic toxicity. TLV-TWA derived from a NOAEL of 300 ppm for reduced WBC counts in a 13 wk inhalation study with rats; a factor of 10 is applied and rounded down to 20 ppm. The value is likely conservative due to anatomical differences in the nasal airways of rats versus humans.  Human data:   * No substance-specific human exposure data; no haematological changes found in workers exposed to mixtures of 1,3-dioxolane and structurally related 1,4-dioxane (no further details provided).   Animal data:   * LC50: 1,056, 22,574, and 28,710 ppm (rats, 4 h); 54,780 ppm (guinea pigs, 4 h); 38,940 ppm (rabbits, 4 h) * Necropsy of rats showed dose-related lung and liver discolouration, bladder distention and gastrointestinal tract damage * Strong eye irritant (rabbits); corneal ulceration, opacity, and iritis noted * Dermal LD50: 15,000 mg/kg (rabbits); no allergenic effects noted in repeat dermal application experiment of same study * Repeat inhalation study with exposure groups 0, 300, 1,000 and 3,000 ppm (rats, 6 h/d, 5 d/wk, 13 wk):   + NOAEC: 300 ppm for reduced white blood cell count and spleen weights; LOAEC: 1,000 ppm   + 3,000 ppm group showed decreased body weight, spleen weights, liver enlargement, bone marrow changes * Dose-related decrease in foetal development rate in reproductive study near maternally toxic levels at 575–1,150 mg/kg by gavage (rats, alternating on GD 8–20)   + maternal toxicity characterised by reduced body weight gain, increased adrenal gland weights, and delayed foetal development   + related fertility study at comparable oral doses reported no effects on male fertility (rats, 5 d/wk, 8 wk) * Microscopic changes to testes and altered spermatogenesis in repeat inhalation study at 825 ppm (rats, 5 h/d, 5 d/wk, 1 yr); only 1 concentration tested * No changes in pups, viability, or litter sizes at 125 ppm in 1-generation inhalational study (rats, 6 h/d, 5 d/wk, 90 d) * Low potential for genotoxicity *in vitro* and *in vivo*; can cause single-strand DNA breaks at 290 mg/kg (rats), but not dose-dependent.   A skin notation not warranted due to evidence for low systemic toxicity in a dermal absorption study with rabbits. Insufficient data for recommending a TLV-STEL or notations for carcinogenicity or sensitisation. |
| DFG 2017 MAK: 50 ppm (150 mg/m3) |
| Summary of additional:  MAK derived from NOAEL of 300 ppm for WBC counts from 13 wk inhalation study with rats (also used by ACGIH, 2018). An overall factor of 4 is applied the NOAEL of 300 ppm and rounded to 50 ppm according to preferred value approach by DFG. Previous MAK of 100 ppm withdrawn following re-evaluation in 2017 despite being based on the same study; rationale for previous value or its reduction to the current MAK is not discussed.  Skin notation retained from previous assessment; 8 h exposure at the previous MAK (100 ppm) ≡3,000 mg assuming a respiratory volume of 10 m3, based on dermal flux calculations an effective dermal dose may reach 1,626 mg assuming a 1 h exposure to 2,000 cm² of skin. Therefore, the dermal route would contribute significantly to overall exposure if the MAK is observed.  Human data:   * Calculated dermal fluxes from 2 studies: 0.348 and 0.813 mg/cm²/h; 1 h exposure to 2,000 cm² of skin ≡696 or 1,626 mg.   Animal data:   * No irritational effects reported at 3,000 ppm in the 13 wk inhalation study the MAK is derived from; critical effects are therefore considered to be systemic   + critical effect is not expected to increase with chronic exposure due to similar haematological findings after wk 4 and 13 of the study * Developmental study with oral dose groups 125, 250, 500 and 1,000 mg/kg/d (rats,  GD 6–15) reported foetal heart and tail malformations, and maternal bw reduction * NOAEL:   + maternal NOAEL: 500 mg/kg/d (rats, oral) for reduced bw gain   + foetal NOAEL: 250 mg/kg/d (rats, oral) for developmental malformations   + findings consistent with a similar, but inadequately conducted, study that reported maternal NOAEL: 580 mg/kg/d and foetal NOAEL: 145 mg/kg/d * Nasal and lung absorption rates of 66.6 and 2.1%, respectively at 500 ppm (dogs, 10 min) * 2 inadequately documented skin sensitisation studies (guinea pigs) had equivocal results; not used in assessment for sensitisation potential * Non-mutagenic *in vitro* equivocal results *in vivo*: slight increase in micronucleus test with bone marrow cells (mice), no dose relationship for single-strand breaks (rats). |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

NIL.

### 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 | — |
| ECHA | NA |
| ACGIH | — |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| 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: |  |  |  | | 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%: | yes | 2.00 |  | |  |  | 2 | **insufficient data to assign a skin notation** | |

### IDLH

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

## Additional information

| Molecular weight: | 74.08 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = Number mg/m3; 1 mg/m3 = Number 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) (2007) 1,3-Dioxolan – MAK value documentation, German language edition.

Deutsche Forschungsgemeinschaft (DFG) (2018) 1,3-Dioxolane – MAK value documentation.