# Morpholine

| CAS number: | 110-91-8 |
| --- | --- |
| Synonyms: | Dimethylineamide oxide, tetrahydro-2H-1,4-oxazine |
| Chemical formula: | C4H9NO |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **20 ppm (71 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **1,400 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 20 ppm (71 mg/m3) is recommended to protect for upper respiratory tract, skin and eye irritation in exposed workers.

## Discussion and conclusions

Morpholine is mostly used in cleaning agents and additives, dishwashing and laundry detergents, corrosion inhibitors and photo chemicals.

The critical effects of exposure are irritation of upper respiratory tract, skin and eyes and corneal oedema (ACGIH, 2018).

Effects are reported as intensely irritating to eyes, mucous membranes and nose following exposure for one minute at 12,000 ppm. Complaints in workers of foggy vision with rings around lights resulting from corneal oedema following exposure to low vapour concentrations for several hours. A sub-chronic study in rats reported eye, skin and mucous membrane irritation at 25 ppm. In a separate study, no reported effects were seen in rats inhaling 25 ppm for 13 weeks (ACGIH, 2018). ACGIH (2018) assign their recommendation based on this study. A NOEC of 10 ppm for nasal irritation is reported in chronic inhalation study in male rats (DFG, 1996; SCOEL, 1999).

A TWA of 20 ppm (71 mg/m3) is recommended to be retained. Minimal irritation of the upper respiratory tract in rats exposed *via* inhalation at 25 ppm, indicates that the recommended TWA is sufficiently low to reduce the risk of irritant effects in exposed workers (ACGIH, 2018). There is insufficient evidence to recommend a STEL.

## 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 recommended based on evidence in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 20 ppm (71 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 20 ppm (71 mg/m3) |
| TLV-TWA recommended to minimise any possible dermal, upper respiratory tract, eye irritation and corneal oedema (no explanation of the derivation).  Summary of data:  Human data:   * Reported as intensely irritating to the eye and mucous membrane of subjects; irritation of nose observed followed exposure to 12,000 ppm for 1 min; coughing after 1.5 min * Reported irritant effects reverse within hours following cessation of exposure * Complaints of foggy vision with rings around lights resulting from corneal oedema following exposure for several hours to low vapour concentrations; no further information * No reports of chronic health effect from occupational exposure.   Animal data:   * LD50: 0.5 mL/kg (rats, dermal) * Eye, skin and mucous membrane irritation was reported in a sub-chronic inhalational study in rats exposed at 25 ppm; a few rats exhibited nasal irritation at 100 ppm; no further information; basis for TLV-TWA * Rats exposed via inhalation for 6 h/d, 5 d/wk for 13 wk: * at 25 ppm, no compound related changes noted * at 100 ppm, focal necrosis and necrotic cell debris in the nasal cavity seen in 2 of 20 rats * at 250 focal erosion and metaplasia in the maxilloturbinates; more severe irritation to the upper respiratory tract with the damage at 13 wk more severe that wk 7.   Insufficient data for RSEN notation and TLV-STEL recommendation. |
| DFG 1996 MAK: 10 ppm (36 mg/m3) |
| Summary of additional data:   * LD50: 500 mg/kg in rats * Previous MAK of 20 ppm set by analogy to other secondary aliphatic amines * No suitable studies in humans to derive MAK value * Chronic inhalation study on the rat: * NOEC of 10 ppm for nasal irritation reported in male rats; basis of MAK * slightly irritating at 50 ppm * clearly irritating at 150 ppm * Based on nasal anatomy, humans not considered to be more sensitive than rats. |
| SCOEL 1999 TWA: 10 ppm (36 mg/m3); STEL: 20 ppm (72 mg/m3) |
| Summary of additional data:   * 13-wk inhalation study in rats; dose finding study for another chronic study (see below): * low incidence of histopathological nasal changes at 360 mg/m3 (100 ppm) * occasional rapid breathing at 90 mg/m3 * NOEC of 36 mg/m3 (10 ppm) (cited by DFG, 1996): * low incidence of histopathological nasal changes was seen at 181 mg/m3 (50 ppm) * TWA based on NOEC of 10 ppm; UF of 1 justified based on mild effects at higher doses * STEL recommended to restrict irritation from peaks; no derivation provided. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | * Rats exposed 6 h/d, 5 d/wk for 104 wk: systemic NOAEC of 543 mg/m3; local NOAEC of 10 ppm (36 mg/m3) for local effects (cited by DFG, 1996). |

### 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 | Skin |
| HCIS | — |
| NICNAS | — |
| EU Annex | NA |
| ECHA | — |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | — |
| SCOEL | — |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 3 |
| US NIOSH | SK:SYS |

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: | yes | 3.00 |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  | 3 | **consider assigning a skin notation** | |

### IDLH

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

## Additional information

| Molecular weight: | 87.1 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 3.56 mg/m3; 1 mg/m3 = 0.281 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) (2000) Morpholin – MAK value documentation.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1999) Recommendation from the Scientific Committee on Occupational Exposure Limits for morpholine. SCOEL/SUM/81.

International Agency for Research on Cancer (IARC) Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide (Part 1, Part 2, Part 3). IARC Monographs – 71.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Morpholine: Human health tier II assessment – IMAP report.

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

US National Institute for Occupational Safety and Health (NIOSH) (2017) NIOSH Skin Notation Profiles: Morpholine.