# Diazomethane

| CAS number: | 334-88-3 |
| --- | --- |
| Synonyms: | Azimethylene, diazirine |
| Chemical formula: | CH2N2 |

Workplace exposure standard (interim)

| TWA: | **2 ppb (3.4 µg/m3)** |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | **Carc. 1B; Sk.** |
| IDLH: | **2 ppm** |
| **Sampling and analysis:** There is uncertainty regarding quantification of the recommended value with available sampling and/or analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 2 ppb (3.4 µg/m3) is recommended to reduce the risk of lung cancer in exposed workers.

Given the limited data available on the mechanism of action for carcinogenicity and its relevance in humans, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

Diazomethane is not produced commercially due to its explosive nature, but is produced and used *in situ* as a methylating agent for acidic compounds such as phenols and carboxylic acids.

There are reports of exposure causing irritation of eyes, dizziness, denudation of mucous membranes and sensitisation in exposed laboratory workers. Chest pains, fever and severe asthmatic attacks are also reported. No other toxicity data exists in humans (ACGIH, 2018).

Diazomethane was found to be carcinogenic in rats and mice under test conditions relevant to worker exposure, which is likely a result of its methylating properties (ACGIH, 2018). Based on evidence in animals, it is considered to be a carcinogen with potential to cause cancer in humans (ACGIH, 2018; DFG, 1999). The current data are insufficient to determine if its carcinogenicity acts *via* a mutagenic mode of action.

Given the carcinogenic potential, a TWA of 2 ppb is derived using the current TWA of 0.2 ppm as a starting point and dividing by 100 to provide an adequate margin of risk.

Investigation of additional data in the next scheduled review is recommended, particularly related to carcinogenicity data.

## Recommendation for notations

Classified as a category 1B 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 of systemic carcinogenic potential following dermal application in animals

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.2 ppm (0.34 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 0.2 ppm (0.34 mg/m3) |
| The TLV-TWA recommended to prevent irritation of the eyes and lower respiratory passages and related toxic effects.  Summary of data:  Human data:   * Exposure has caused irritation of eyes, dizziness, denudation of mucous membranes and sensitisation in laboratory workers * Case reports of chest pains, fever and severe asthmatic attacks (no further information).   Animal data:   * 175 ppm for 10 min fatal to cats within 3 d * Exposure of guinea pigs produced severe respiratory tract irritation and pulmonary oedema (no further information) * Toxicity in rats comparable to phosgene and related to its strong methylating agent * 13 rats exposed for 4.5–6 mo to diazomethane gas: * 7 rats survived longer than 10 mo with 3 presenting pulmonary adenomas * 1/3 also had a squamous-cell carcinoma of the lung (no further information) * 12 mice skin painted 5 times/wk for 5 mo with liquid diazomethane: * all 8 that died between 5 and 12 mo had lung adenomas * Limited but consistent evidence of lung adenomas in mice and pulmonary adenomas and squamous carcinomas in rats; relevant to occupational exposure route.   Insufficient evidence to recommend skin or SEN notations or a TLV-STEL.  No information on derivation of TLV-TWA. |
| DFG 1999 Not assigned |
| Summary of additional data:   * No MAK recommended due to carcinogenic effects in rodents * Highly mutagenic in *E. coli* * Positive in mutagenicity test with *Saccharomyces cerevisiae* and in two other mutagenicity tests (no further information) * When DNA was incubated with diazomethane *in vitro*, DNA-methylation could be detected * Carcinogenicity likely due to methylating properties * Unclear results in sensitising test in guinea pigs. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 2002 | * Did not identify any critical new studies. |
| NIOSH |  | 1996 | * IDLH based on analogy to phosgene. |

### 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 | Carc. 1B |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | NA |
| EU Annex | Carcinogenicity – category 1B |
| ECHA | Carc. 1B |
| ACGIH | Carcinogenicity – A2 |
| DFG | — |
| SCOEL | NA |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 3 |
| 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 |
| --- |
| Insufficient date available, however there is evidence of systemic carcinogenic potential following dermal application in animals. |

### IDLH

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

## Additional information

| Molecular weight: | 86.09 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 1.72 mg/m3; 1 mg/m3 = 0.582 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) (1999) Diazomethane – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Diazomethane – REACH assessment.

International Agency for Research on Cancer (IARC) (1987) Diazomethane. IARC Monographs on the evaluation of the carcinogenic risk to humans.

Tenth Adaptation to Technical Progress Commission Regulation (EU) 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).

US Environmental Protection Authority (US EPA) (2002) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Diazomethane.

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