# Ethylenimine

| CAS number: | 151-56-4 |
| --- | --- |
| Synonyms: | Aminoethylene, aziridine, dimethyleneimine |
| Chemical formula: | C2H5N |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **5 ppb** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1B, Sk.** |
| IDLH: | **—** |
| **Sampling and analysis:** The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 5 ppb is recommended to protect for cancer in exposed workers.

Due to uncertainty regarding the data, it is recommended a further, in-depth assessment of the toxicological and epidemiological data for the chemical be undertaken.

## Discussion and conclusions

## Ethylenimine is used as an intermediate and monomer for oil additive compounds, ion exchange resins, coating resins, pharmaceuticals, adhesives, polymer stabilisers and surfactants.

Critical effects of exposure include upper respiratory tract irritation, damage to the liver and kidney and systemic tumour formation. Based on evidence in animals of tumour formation in different sites following oral, subcutaneous and intragastrical administration, it is considered a confirmed animal carcinogen and possible human carcinogen (ACGIH, 2018; DFG, 2003; NICNAS, 2014). It is also reported to have high degree of mutagenic activity in a wide variety of systems (ACGIH, 2018). There are insufficient data to ascertain mechanism of tumour formation and therefore for the purpose of this assessment, ethylenimine is considered a non-threshold-based genotoxic carcinogen until further data are available.

At present, an Inhalation Unit Risk or Oral Slope Factors could not be identified to derive a TWA. As such, the current TWA of 0.5 ppm is considered a suitable starting point. Dividing this starting point by compound uncertainty factor of 100 as a precautionary measure, for interspecies uncertainty and severity of potential effects and to provide an adequate margin of safety results in a recommended TWA of 5 ppb. This TWA is recommended in interim to protect for adverse effects in exposed workers. A STEL is not recommended as the TWA is sufficiently low to protect for acute effects from short-term concentration excursions.

Due to the uncertainty associated with the limited information available in the primary sources, it is recommended a further, more in-depth assessment of the toxicological and epidemiological data for the chemical be undertaken at the next scheduled review.

## 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 effects following dermal exposure in humans and animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.5 ppm (0.88 mg/m3) | |
|  |
| ACGIH 2009 TLV-TWA: 0.05 ppm (0.09 mg/m3) TLV-STEL: 0.1 ppm (0.18 mg/m3) |
| TLV-TWA recommended to minimise the potential for upper respiratory tract irritation and liver and kidney effects in workers.  Derivation of TWA and STEL not provided; this TWA is not substantiated.  Summary of data:  Human data:   * Acute accidental exposure of 5 people for ≈2 h in a poorly ventilated room; effects delayed several hours included: * throat soreness, severe eye irritation, vomiting and coughing, conjunctivitis, upper and lower respiratory tract inflammation * transitory polycythaemia, leucocytosis, eosinophilia and albuminuria * symptoms subsided within 6 mo * Case report of several fatalities resulting from combined inhalation and skin contamination: * pneumonia and pulmonary oedema within 2–3 h after brief exposures * one case 5 min exposure resulted in progressive respiratory obstruction from destruction of the tracheobronchial cartilage over a period of 2 mo * Acute inhalation or dermal exposure of workers resulted in CNS effects, excess fluid in the lungs, damage to the liver and kidneys and in some cases, death (no further information).   Animal data:   * LC50: 15 ppm (rats, 8 h) * LD50: 13 mg/kg (rabbits, dermal) * Exposure ≥10 ppm (guinea pigs and rats, 8 h) resulted in extreme respiratory difficulty * Daily inhalation of 5 ppm for 1.5 mo; catarrhal bronchitis, diminishing of lymphatic elements in lymph glands and degenerative changes in liver and kidneys of rats * Subcutaneous injection site sarcomas and fibromas in rats * Gavage administration of 4.64 mg/kg/d for 7–28 d, followed by 13 ppm in the diet (equivalent dose in mg/kg/d not provided) for 74 wk resulted in pulmonary and hepatic tumours in mice; no further information * Reported high degree of mutagenic activity in a wide variety of systems: * mutagenic in *Drosophila melanogaster, Neurospora crassa and Saccharomyces cerevisiae* * reacts with *E. coli* DNA *in vitro* to yield mutant forms * strongly mutagenic to Chinese hamster ovary cells *in vitro* and murine bone marrow cells *in vivo* * induced large numbers of chromatid type aberrations *in vitro* in human WI-36 cells and leukocytes.   Insufficient data to recommended sensitiser notation. |
| DFG 2003 Not assigned |
| No MAK recommended due to carcinogenic potential.  Summary of additional data:   * Known strong alkylating effect * Caused liver and lung tumours in two different mouse strains in an oral toxicity study; gavage in a total amount of 4.64 mg/kg/d from 7 to 28 d of life, then 13 ppm in diet (equivalent dose in mg/kg/d not provided) for 74 wk (cited by ACGIH, 2018): * males: 16/17 (15 hepatomas, 15 lung tumours) and 16/16 (9 hepatomas, 12 lung tumours) * females: 15/15 (11 hepatomas, 15 lung tumours) and 11/11 (2 hepatomas, 10 lung tumours, 2 lymphomas) * considered development of tumours as result of systemic availability * An increased incidence of lung tumours in male rats following single subcutaneous injection * Mutagenic in the *S. typhimurium* test without S9 mix * Carcinogenic, mutagenic and DNA damaging effects under conditions comparable to the potential exposure of humans in the workplace. |
| 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 |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * Tumours at several different tumour sites (lung, liver, mammary gland) in rats and/or mice following oral and inhalation exposure and administration by subcutaneous injection * Formation of DNA adducts has been demonstrated *in vitro* * Genotoxic mode of action for carcinogenicity cannot be excluded. |
| US EPA |  | 1992 | * Health effects data inadequate for an inhalation RfC * Not undergone a complete evaluation and determination for evidence of human carcinogenic potential. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Yes |
| **The chemical is a non-threshold based genotoxic carcinogen.** |  |
| Is a cancer slope factor or inhalation unit risk value available? | No |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 1B, Skin |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat 2, Skin |
| EU Annex | NA |
| ECHA | Carc. 1B |
| ACGIH | Skin, Carcinogenicity – A3 |
| DFG | Carcinogenicity – 2, H (skin) |
| SCOEL | NA |
| 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Adverse effects in human case study: | Yes | 4.00 |  | | 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 | **a skin notation is warranted** | |

### IDLH

| Is there a suitable IDLH value available? | No, the chemical is a genotoxic carcinogen |
| --- | --- |

## Additional information

| Molecular weight: | 43.07 |
| --- | --- |
| 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) (2003) Ethylenimin – MAK value documentation.

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

International Agency for Research on Cancer (IARC) (1999) Aziridine. IARC Monographs on the evaluation of the carcinogenic risk to humans.

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