# 2,2’-Oxybis[ethanol]

| CAS number: | 111-46-6 |
| --- | --- |
| Synonyms: | Diethylene glycol, 2-(2-hydroxyethoxy)ethane-2-ol, bis(2-hydroxyethyl) ether, Brecolane ndg,  Deactivator H, Dicol |
| Chemical formula: | C4H10O3 |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **23 ppm (100 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 23 ppm (100 mg/m3) is recommended to protect for kidney damage in exposed workers.

## Discussion and conclusions

2,2’-Oxybis[ethanol] is used in the manufacture of resins, as a component of anti-freeze, in cosmetic ingredients and in brake fluids and lubricants (ECHA, 2019; NICNAS, 2013).

Critical effects of exposure are kidney and liver damage.

Irritation of the throat and face is reported in a study of volunteers exposed to 140 mg/m3. An exposure greater than 200 mg/m3 is not tolerated for more than a minute. No further human inhalation data are available (ECHA, 2019). Humans appear more susceptible to acute toxic effects than animals (DFG, 1995). A NOAEL of 50 mg/kg/day for oxalate formation in rats reported by DFG (1995) used for MAK derivation. This is disputed by HCOTN (2007), NICNAS (2013) and ECHA (2019) as elevated oxalate formation is not considered a toxicity indicator. These sources report a NOAEL of 300 mg/kg/day from the same study based on histopathological findings in the kidney and liver (hydropic degeneration of the kidneys and tubular necrosis in the kidneys resulting in renal failure).

Based on the weight of evidence presented, the SWA TWA of 23 ppm (100 mg/m3) is recommended to be retained and is considered protective of potential kidney damage after chronic exposure and irritation effects after acute exposures.

## 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, noting there is conflicting data between agencies.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA Year TWA: 23 ppm (100 mg/m3) | |
|  |
| ACGIH NA NA |
| No report. |
| DFG 1995 MAK: 10 ppm (44 mg/m3) |
| MAK recommended to protect for liver and kidney effects.  Summary of data:   * Acute toxicity ≈10 times higher in humans than in animals.   Human data:   * Mass intoxication following repeated intake during sulphonamide preparation (containing 72% 2,2’-oxybis[ethanol] as solvent), 71 adults and 41 children died: * headaches, dizziness and vomiting, clinical signs of kidney damage, followed by kidney failure * doses from ≈16–190 g (adults) * smallest lethal dose calculated ≈1,100 mg/kg bw * Tolerated for 48 h in volunteers with no irritation in patch test, concentration of 20% in Vaseline.   Animal data:   * No deaths following 4 h exposure at 4,500 mg/m3 in rats * LD50: 10,000–27,000 mg/kg/d (rats, mice and dogs, oral); ≈8,700 mg/kg/d (guinea pigs, oral); ≈4,930 mg/kg/d (rabbits, oral) * LD50: ≈13,300 mg/kg/d (rabbit, dermal) * No skin irritation after repeated application in rats and guinea pigs * No irritation of rabbit eye * No evidence of sensitisation in guinea pigs * NOEL: 50 mg/kg/d (male and female rats, gavage); 2 studies: 99 d with doses 300, 1,500 and 3,300 mg/kg/d and 225 d with doses 50, 100, 300, 1,500 mg/kg/d: * oxalate crystals in urine * slight kidney effects * NOEL: 750 mg/kg/d (male and female rats, gavage, 28 d); doses 0, 38, 188, 750 and 3,300 mg/kg/d: * oxalate crystals in urine of males and reduced brain weights in females * effects reversible * Difference in NOELs of rat studies unclear * No evidence of genotoxic potential * No evidence of direct carcinogenic effect in rat and mice studies; indirect effect of high doses is bladder stones, can induce bladder tumours.   Utilising NOEL of 50 mg/kg/d as starting point, a safety margin of 10 was applied to derive MAK. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA 2016 TWA: 10 mg/m3 |
| No additional data. |
| HCOTN 2007 Not assigned |
| Summary of additional data:   * Likely routes of exposure are contact with skin and eyes during industrial handling * Aerosol also an exposure concern, resulting in GIT absorption * Metabolite likely responsible for adverse effects on kidney * Due to significant systemic toxicity, committee recommends skin notation (based on data from SkinPerm model).   Based on histopathological findings, including hydropic degeneration of the kidneys and tubular necrosis in the kidneys (resulting in renal failure), committee concludes HBROEL should be derived from NOAEL of 300 mg/kg/d (based on same study cited in DFG, 1995, which identified NOAEL of 50 mg/kg/d but HCOTN dispute identity of crystals in urine, and therefore higher NOAEL derived). Application of UF of 10 for interspecies differences and 3 for intraspecies differences, results in recommended TWA of 70 mg/m3 (16 ppm) (assuming 70 kg worker and 10 m3 respiratory volume per 8 h shift).  TWA applies to sum of concentrations existing as vapour and aerosol. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | * NOAEL of 50 mg/kg/d (cited in DFG, 1995) called into question as elevated oxalate formation not considered toxicity indicator: * NOAEL of 300 mg/kg/d therefore identified based on histopathological findings and 100 mg/kg/d based on increased urine volume * Neurologic effects noted in severe intoxications * Large-scale intoxication of children following ingestion of contaminated paracetamol syrup; median lethal dose based on acute renal failure 1,490 mg/kg/d * Based on weight of evidence from *in vitro* and *in vivo* studies, not considered genotoxic and not considered carcinogenic. |
| ECHA |  | 2019 | * NOAEL utilising increased oxalate crystals and urine volume also questioned; NOAEL determined to be 300 mg/kg/d based on histopathological findings * Volunteers exposed at 3–67 mg/m3 (aerosolised) for 20–22 h/d for 1 mo; not tolerated for more than 1 min at ≥200 mg/m3; irritation of throat and faces commonly reported at 140 mg/m3 * Based on available data, no evidence of genotoxic or mutagenic properties; not considered carcinogenic * DNEL = 44 mg/m3 (based on DFG) for long-term systemic effects. |

### 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 | NA |
| HCIS | — |
| NICNAS | — |
| EU Annex | NA |
| ECHA | — |
| ACGIH | NA |
| DFG | — |
| SCOEL | NA |
| HCOTN | Skin |
| 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: | no |  |  |
| 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 |  |  |
|  |  |  | **Insufficient data to assign a skin notation** |

### IDLH

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

## Additional information

|  |  |
| --- | --- |
| Molecular weight: | 106.12 |
| 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

Deutsche Forschungsgemeinschaft (DFG) (1995) Diethylene glycol – 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).

Health Council of the Netherlands (HCOTN) (2007) Diethylene glycol. Health-based recommended occupational exposure limit. The Hague: Health Council of the Netherlands; publication no. 2007/03OSH.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) Ethanol, 2,2-oxybis-: Human health tier II assessment – IMAP report.

Occupational Alliance for Risk Science (OARS) (2016) Workplace environmental exposure level – Diethylene Glycol.