# Chlorine dioxidE

| CAS number: | 10049-04-4 |
| --- | --- |
| Synonyms: | Chlorine peroxide, chlorine oxide, chlorine(IV) oxide, chloryl |
| Chemical formula: | ClO2 |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **—** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **0.1 ppm** |
| Notations: | **—** |
| IDLH: | **5 ppm** |
| Sampling and analysis: | The recommended value is quantifiable through available sampling and analysis techniques. |

## Recommendation and basis for workplace exposure standard

A peak limitation of 0.1 ppm (0.28 mg/m3) is recommended to protect for acute upper respiratory tract irritation and lung oedema in workers.

## Discussion and conclusions

Chlorine dioxide is a gas under standard conditions that hydrolyses readily in contact with moisture. It has been used for disinfection, sterilisation, bleaching and chemical manufacture.

Critical effects of exposure are irritation to the respiratory tract and pulmonary dysfunction. A peak limitation is recommended due to the steep dose-response relationship observed in a case study of workers at a sulfite cellulose plant that reported a NOAEL for respiratory tract irritation of 0.1 ppm. This is supported by reports of bronchitis and pulmonary dysfunction in workers exposed to an average of 0.25 ppm and a NOAEL of 0.1 ppm for respiratory effects in sub-chronically exposed rats (ACGIH, 2018; DFG, 2000).

Most available data of systemic toxicity relate to exposure through oral routes (e.g. in drinking water due to its use in sanitation), which may not translate to inhalational exposures in the workplace (ACGIH, 2018). A detailed examination of the available inhalational data should be prioritised during subsequent reviews.

## 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 not recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA Year TWA: 0.1 ppm (0.28 mg/m3); STEL: 0.3 ppm (0.83 mg/m3) | |
|  |
| ACGIH 2018 TLV-Ceiling: 0.1 ppm (0.28 mg/m3) |
| TLV-Ceiling intended to protect for respiratory tract irritation and lung oedema.  Human data indicates a steep dose-response relationship and supports recommendation of a TLV‑Ceiling. Insufficient data to recommend notations for carcinogenicity, skin absorption or sensitisation.  Summary of data:  Toxicity from oral administration not considered relevant to workplace exposures. Assessed literature refers primarily to inhalational routes. Skin contact is a minor exposure route and not considered in the development of the TLV-Ceiling. No human or animal carcinogenicity studies available.  Human data:   * Irritation at 5 ppm and lethal at 19 ppm (unspecified duration) * Case study of sulfite cellulose plant workers reported typical exposures to ClO2 of <0.1 ppm with co-exposures to Cl2 of ≈1 ppm over 5 yr:   + eye and respiratory tract irritation and resulting bronchitis reported in 7/12 workers   + GIT irritation also reported   + all effects attributed to short exposures >0.1 ppm and in the presence of Cl2   + no effects attributed to exposure at ≤0.1 ppm * Exposures at 0–0.2 ppm associated with chronic bronchitis in mill workers   + also exposed to SO2 and Cl2 at unknown concentrations * A number of case studies suggest assessment of adverse effects are confounded by the absence of exposure levels or by mixed exposures to O3, SO2 and Cl2.   Animal data:   * Several sub-chronic repeat exposure studies (13 d to 10 wk) have been carried out with rats: * respiratory distress, decreased body weight and bronchopneumonia reported at decreasing weekly doses from 3,400–800 ppm (3 min/d, 1 d/wk, 3 wk) * rhinorrhoea, rapid shallow breathing and weight loss in exposed animals at 10 ppm (4 h/d, 9/13 d); respiratory infection and acute renal and hepatic congestion observed * NOAEL: 0.1 ppm for these effects (5 h/d, 10 wk) * LOAEL: 2.5 ppm for adverse lung effects (7 h/d, 30 d); same LOAEL in rabbits (4 h/d, 45 d) * NOAEL: 5 ppm for alveolar lesions (15 min/d, 2 or 4 times/d, 4 wk); LOAEL of 10 ppm, alveolar damage in 15 ppm exposure group was reversible within 15 d following exposure * Lowest lethal concentration (LCLO): 500 ppm (rats, 15 min) * LD50: 39-113 mg/kg (rats, oral) * Hyperplasia in mice exposed (full body) to aqueous solutions at 300–1000 mg/L over 1–4 d * Pulmonary oedema, epistaxis, circulatory engorgement, and ocular discharge at 260 ppm in single dose inhalation study (rats, 2 h); 1 of 4 rats died * Weakly mutagenic based on available genotoxicity data; induction of micronuclei in mice following intraperitoneal injection, positive result in Ames test, negative in unspecified chromosomal test * Lowest effective dose of 0.2 ppm for genotoxic response in human leukocytes, 5 ppm in *Saccharomyces cerevisiae*. |
| DFG 2000 MAK: 0.1 pm (0.28 mg/m3) |
| Summary of additional information:  MAK derived from NOAEL of 0.1 ppm for pulmonary effects in rats as reported in ACGIH, 2018 and maintained provisionally. No data presented on allergenic effects.  Human data:   * Obstructive pulmonary dysfunction and mild bronchitis also reported in individuals exposed to average concentrations of 0.25 ppm (unknown duration).   Animal data:   * LC50: 32 ppm (rats, 4 h); death from emphysema and oedema * LD50 >2,000 mg/kg (rats, dermal); occlusive dermal patch of 5% aqueous solution for 24 h, death occurred 4 d following exposure * Thyroid hormone imbalance in rats and monkeys at 9 mg/kg/d when administered in drinking water * Conflicting mutagenicity results from *in vitro* studies: non-mutagenic in Ames test and in Chinese hamster ovary cells, but dose-dependent induction of mutations in a mouse lymphoma cell test without metabolic activation * Non-mutagenic *in vivo* * No effect on fertility and does not cause teratogenicity or embryo or foetal toxicity in rats * No clinical effects following full body exposure at 2.33 ppm (rats, 4 h) * NOAEL: 100 mg/L for haematological changes, administered in drinking water (mice, 30 d). |
| 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 |
| --- | --- | --- | --- |
| HSE |  | 2002 | * 8 h TWA: 0.1 ppm (0.28 mg/m3) * 15-min STEL: 0.3 ppm (0.84 mg/m3) |
| APVMA |  | 2002-2018 | * Used as a sanitiser and swimming pool disinfectant |
| US EPA |  | 2000 | * LOAEL: 2.5 ppm for adverse lung effects in rats and rabbits (respectively 7 h/d, 30 d or 4 h/d, 45 d), as presented in ACGIH, 2018 used as principal study to derive inhalation reference concentration * No satisfactory human or animal studies assessing the chronic carcinogenic potential of chlorine dioxide have been available * Concentrates prepared from drinking water treated with chlorine dioxide did not increase the incidence of lung or skin tumours in mice and rats. However, hyperplasia reported in mouse skin * Genotoxicity studies are equivocal. |
| US NIOSH |  | 1994 | * IDLH is based on acute inhalation toxicity data in humans. |

### 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 | — |
| HCIS | — |
| NICNAS | — |
| EU Annex | — |
| ECHA | NA |
| ACGIH | — |
| DFG | — |
| 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: | 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%: |  |  |  | |  |  |  | **a skin notation is not warranted** | |

### IDLH

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

## Additional information

| Molecular weight: | 67.46 |
| --- | --- |
| 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.

Australian Pesticides & Veterinary Medicines Authority (APVMA) (2018) Agricultural Chemical Products and Approved Labels, gazette No. 12.

Deutsche Forschungsgemeinschaft (DFG) (2000) Chlordioxid – MAK value documentation, German language edition.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Chlorine oxide:

Human health tier I assessment – IMAP report.

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

UK Health and Safety Executive (HSE) (2002) EH40/2005 Workplace exposure limits.

US Environmental Protection Authority (US EPA) (2000) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Chlorine dioxide.