# Zirconium compounds (as Zr)

| CAS number: | 7440-67-7 |
| --- | --- |
| Synonyms: | — |
| Chemical formula: | Zr |

Workplace exposure standard (interim)

| TWA: | **5 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **25 mg/m3** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 5 mg/m3 is recommended to protect for impaired lung function and radiographic changes in the lungs in exposed workers.

Insufficient data are available to recommend a STEL.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

Zirconium compounds are used in nuclear technology, photography, high-vacuum and medical applications and ceramic and coatings manufacture.

The critical effects of exposure are impaired lung function and radiographic changes in the lungs.

The available toxicological database is limited. Toxicity is dependent on solubility of the individual compounds (DFG, 1999). Air concentrations of 1.4–3.4 mg/m3 are not associated with adverse effects in exposed workers in several workplace studies (ACGIH, 2018; DFG, 1999; HCOTN, 2002). Reports of dermal respiratory hypersensitivity in humans and animals resulting in allergic granulomas are equivocal and specific to certain zirconium compounds (ACGIH, 2018; DFG, 2002; HCOTN, 2002). In sub-chronically exposed rodents, slight fibrotic changes in the lungs are associated with exposure to soluble and insoluble zirconium compounds at a LOAEC of 4.7 mg/m3 and 5.4 mg/m3 as Zr, respectively (DFG, 1999; HCOTN, 2002); and not at 3.5 mg/m3 in a chronic inhalation study with rats exposed to either soluble or insoluble compounds (ACGIH, 2018). Exposure to soluble zirconium tetrachloride, which produces hydrogen chloride upon hydrolysis, at 6 mg/m3 caused slight changes in haematology in dogs and increased mortality in rodents (ACGIH, 2018).

DFG (1999) does not recommend a MAK for the soluble compounds due to a lack of adequate data and recommends a MAK of 1 mg/m3 for insoluble compounds based on a LOAEC of 5.4 mg/m3 in rodents, supported by a NOAEC of 1.4 mg/m3 in humans. HCOTN (2002) considers these data insufficient to recommend a health-based OEL or to comment on the suitability of the administrative OEL of 5 mg/m3. The TLV-TWA and TLV-STEL are based on the LOAEC of 6 mg/m3 in animals and expected to be sufficiently low to protect for respiratory irritation. However, no evidence for irritation endpoints is reported in the ACGIH assessment. In view of these uncertainties and limited toxicological information, the TWA of 5 mg/m3 of SWA and ACGIH is recommended to be retained in the interim and further assessment of additional sources is recommended during subsequent reviews of the WES.

There are insufficient data to indicate acute effects within an order of magnitude of the TWA, the STEL of 10 mg/m3 is therefore withdrawn.

## 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. However, the recommendations for dermal and respiratory sensitiser notations are inconsistent in the source material. DFG (1999) recommends dermal and respiratory sensitiser notations based on positive responses in humans and animals, whereas ACGIH (2018) and HCOTN (2002) consider the available database as insufficient for classification.

There are insufficient data to recommend a skin notation.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 mg/m3; STEL: 10 mg/m3 | |
|  |
| ACGIH 2001 TLV-TWA: 5 mg/m3; TLV-STEL: 10 mg/m3 |
| TLV-TWA and TLV-STEL intended to protect for respiratory tract irritation. Not classifiable as a human carcinogen (A4) based on absence of increased tumorigenicity in chronic feeding studies with rats.  Summary of information:  Available animal and human data indicate low toxicity. TLV-TWA and TLV-STEL based on results of inhalation studies with animals, indicate no effects at 11 and 75 mg/m3 for the oxide and slight increase in mortality due to respiratory infection at 6 mg/m3 for the tetrachloride, the effects likely caused by the HCl product. No further details on derivation of TLVs provided.  Human data:   * Typical daily dietary dose ≈4 mg * No adverse effects in exposed workers (n=22, 1–5 yr duration, no details on exposure provided) * Allergic granulomas on axillary skin reported from deodorant or poison ivy remedy use; products contained sodium zirconium lactate or zirconium dioxide * No granulomas observed in controlled patch test using zirconium oxychloride (n=54).   Animal data:   * No significant changes in mortality, growth rate, blood chemistry, urinary proteins, haematology and histopathology at 11 and 75 mg/m3 of zirconium oxide (rats, rabbits, guinea pigs, dogs, cats, 6 h/d, 5 d/wk, 30 or 60 d):   + slight (no details on statistical significance provided) reductions in haemoglobin and RBC count at 6 mg/m3 of zirconium tetrachloride (dogs) and increased mortality (rats, guinea pigs); effects likely caused by production of HCl from hydrolysis of zirconium tetrachloride; cause of death likely due to respiratory infection * No effects on relative organ weights, mortality and tumorigenicity at 5 ppm of diet in chronic feeding study (rats, lifetime); substance accumulated in spleen without adverse effects:   + poor oral bioavailability considered responsible for lack of toxicity from chronic feeding * No adverse effects at 3.5 mg/m3 of zirconium oxide or tetrachloride in separate chronic inhalation studies (rats, 1 yr, no details on exposure duration or frequency provided).   Insufficient data to assign notations for skin absorption and sensitisation. |
| DFG 1998 MAK for insoluble compounds: 1 mg/m3 (inhalable fraction)  MAK for soluble compounds: not established |
| Summary of additional information:  Insoluble and soluble zirconium compounds assessed separately due to higher toxicity of soluble compounds. Critical effects of exposure to insoluble compounds are granulomatous and fibrotic lung changes; soluble compounds cause tissue degeneration at exposed sites and haematological changes.  *Insoluble compounds*  MAK of 1 mg/m3 based on LOAEC of 5.4 mg/m3 for interstitial pneumonitis and slight fibrogenic effects in sub-chronically exposed rodents using barium zirconate; recommendation supported by NOAEC of 1.4 mg/m3 for lung function and radiographic changes in exposed workers.  *Soluble compounds*  MAK not established based on LOAEC of 4.7 mg/m3 for interstitial pneumonitis and slight fibrogenic effects in rodents exposed sub-chronically to zirconium lactate and increased mortality at 6 mg/m3 in rodents sub-chronically exposed to zirconium tetrachloride (also reported in ACGIH, 2018)  Sensitiser notation recommended based on evidence for allergic granulomas following dermal and respiratory sensitisation in humans and animals.  Human data:   * Lung half-life: 224 d; excreted in urine and faeces * No significant radiographic changes or lung function impairment in production workers exposed at 0.7–3.2 mg/m3 (n=32, 1–17 yr duration) * No pulmonary granulomas, but mild bronchial asthma in 2 workers and chronic bronchitis in 5 workers exposed to zirconium chloride, zirconium oxide and metallic zirconium; co-exposure to chlorine could not be excluded as cause for adverse effects * No abnormalities in radiographs or lung examinations in workers (n=5) exposed at ≈1.4–3 mg/m3 for 1–4 yr * Allergic alveolitis in exposed welder in nuclear technology industry, histopathologic lung examination showed foreign body-induced granulomatosis and fibrotic changes; foreign bodies contained zirconium:   + similar allergic granulomatous changes observed in mammary glands and axillary lymph nodes of worker * Epithelial cell granulomas in 1/30 volunteers following dermal application of 5% solution (5 min/d, 8 wk) and in 2/20 volunteers with 10% solution * No reports of contact dermatitis.   Animal data:   * Whole-body half-life: 328–365 d (dogs) * Increased lung weights and diffuse interstitial pneumonitis with slight fibrogenic effects at 4.7 and 36 mg Zr/m3 as zirconium lactate or 5.4 mg Zr/m3 as barium zirconate (rats, hamsters, guinea pigs, 7 h/d, 5 d/wk, 225 d) * Non-sensitising in standardised skin sensitisation test (guinea pigs) and lymph node assay study (mice) with zirconium tetrachloride * Delayed hypersensitivity reactions and nodular granulomas identified in sensitisation study using sodium zirconium lactate; induction with 1.25 mg/kg followed by provocation after 2 wk with 25 µg solution 1 d/wk for 5 wk * Non-mutagenic *in vitro* in bacteria, increased chromosomal aberrations and sister chromatid exchange in human blood cells.   Insufficient data to recommend notations for carcinogenicity or skin absorption. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2002 TWA: 5 mg/m3 |
| Summary of additional information:  Critical effects are lung fibrosis and allergic granulomatosis. Agency considers database insufficient to assess suitability of current administrative OEL of 5 mg/m3. Certain compounds, including sodium zirconium lactate, zirconium aluminium glycinate, were sensitising to skin in animals and humans; however, zirconium tetrachloride was not.  Human data:   * No increase in mortality from all causes in antimony smelter workers exposed exclusively to zirconium silicate * No evidence for cumulative effects from zirconium dust exposure including radiographic changes and lung function impairment in workers exposed at 3.4 mg/m3 (n=178, average duration 10 yr) * No significant radiographic changes found in exposed workers reported in 1 study (n=32, 1–17 yr duration, also reported in DFG, 1999); HCOTN does not consider results in its evaluation due to co-exposure to silicon carbide.   Animal data:   * Sub-chronic inhalation study with exposure at 4.7 and 36 mg Zr/m3 as zirconium lactate or 5.4 mg Zr/m3 (rats, hamsters, guinea pigs, 7 h/d, 5 d/wk, 225 d, also reported in DFG, 1999) not considered in evaluation due to limited study design * Positive mutagenicity *in vitro* in bacteria and human leukocytes; chromosomal aberrations at oral doses of 220–2,250 mg/kg *in vivo* (mice). |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| ECHA |  | 2020 | * DNEL adopted from ACGIH (2018) TLV-TWA recommendation in the absence of additional information. |
| US NIOSH |  | 1994 | * IDLH based on acute toxicity data in animals. |

### 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 | NA |
| EU Annex | — |
| ECHA | — |
| ACGIH | Carcinogenicity – A4 |
| DFG | Sa (respiratory sensitiser), Sh (dermal sensitiser) |
| SCOEL | NA |
| HCOTN | — |
| 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

Insufficient data to assign a skin notation.

### IDLH

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

## Additional information

| Molecular weight: | 91.224 u |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = NA mg/m3; 1 mg/m3 = NA 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) (1998) Zirconium and its compounds – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2002) Zirconium and zirconium compounds. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/059.

European Chemicals Agency (ECHA) (2020) Zirconium – REACH assessment.

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