# Arsenic and compounds (exCept Arsine)

| CAS number: | 7440-38-2 (elemental) |
| --- | --- |
| Synonyms: | **—** |
| Chemical formula: | As |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **0.01 mg/m3 (as As)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1A** |
| IDLH: | **5 mg/m3 (as As)** |
| Sampling and analysis: | There is uncertainty regarding quantification of the recommended value with currently available sampling and/or analysis techniques. |

## Recommendation and basis for workplace exposure standard

A TWA of 0.01 mg/m3 is recommended to protect for excess skin, lung and liver cancers in exposed workers. There are insufficient data to recommend a STEL or peak limitation.

An assessment of mutagenicity is complicated by the variety of compounds within the arsenic group. A detailed examination of these data is recommended to be prioritised during subsequent reviews.

## Discussion and conclusions

Arsenic is typically encountered as compounds in pesticides, starting materials for alloy and semiconductor production, and specialty glass production. It is a carcinogen in humans. The critical effects of bioavailable arsenic are cancers of the skin, liver and lungs, systemic arteriosclerosis, cirrhosis of the liver and congestion and disease of the upper respiratory tract. A mutagenic mechanism of action is not established for arsenic compounds due to the inconsistent results from *in vitro* and human studies (ACGIH, 2018; DFG, 2017).

The TWA is based on an epidemiological study of arsenic exposed workers in which the lowest exposure level associated with an excess risk of lung cancer is 0.2 mg/m3. A no effect level for cancer risk for these compounds has not been established (ACGIH, 2018). A factor of 20 was applied to account for uncertainties in mutagenicity data and no clear NOAEL for carcinogenic effects.

## Recommendation for notations

Arsenic compounds are classified as category 1 carcinogens according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Arsenic compounds are not classified as skin or respiratory sensitisers according to the GHS.

A skin notation is not recommended for arsenic compounds as there is no evidence of systemic effects resulting from skin absorption.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA Year TWA: 0.05 mg/m3 (as As) | |
|  |
| ACGIH 2001 TLV-TWA: 0.01 mg/m3 (as As) |
| TLV-TWA recommended to minimise adverse effects to the skin, liver, peripheral nerves and vasculature, upper respiratory tract and lungs. Adverse effects include cancers of the skin, liver and lungs, systemic arteriosclerosis, cirrhosis of the liver, and upper respiratory tract disease.  Insufficient data to derive a STEL; available data does not warrant skin or sensitiser notations.  Classified as a confirmed human carcinogen.  Summary of data:  The TLV-TWA is based on epidemiological data that suggests the lowest exposure level associated with an excess risk of lung cancer is 0.2 mg/m3; a no effect level for risk exists has not been established. A factor of 20 is applied to account for the current lack of evidence for a level at which no risk of cancer exists.  Human data:   * Half-life of 24–36 h in humans * Epidemiological study of NaAsO2 production workers at a single factory found excess respiratory and skin cancers causing death in workers with highest exposures to As; atmospheric concentration ranged from a median of 0.07 mg/m3 (packing area) to a median of 0.7 mg/m3 (grinding area). * Multiple epidemiological studies conducted at a copper smelter suggest a causal relationship between As exposure and lung cancer (Montana group; overall 8,000 workers) * one of these studies (SMR study of 1,800 workers) demonstrated excess lung cancers in workers exposed to high concentrations of As * SMR increased from 138 in lowest exposure group (<0.1 mg/m3) to 704 in highest exposure group (>5 mg/m3) * Positive relationship between time‑weighted exposure and risk of lung cancer in SMR study of a copper smelter (Tacoma group: 2,800 workers) * excess risk of respiratory cancer in lowest exposure group (0.2 mg/m3) based on atmospheric exposure (type not specified) and urine sampling * Clinically non-relevant changes to liver function in As2O3 workers exposed to  5.7–11.6 µg/m3 (82.6 µg/L urinary excretion) compared with smelter workers exposed to 18.9 µg/m3 (53.3 µg/L urinary excretion) * Noted higher urinary concentration in As2O3 workers than smelter workers despite their lower airborne As exposure * Currently available mutagenicity data from patients and exposed workers is inconsistent.   Animal data:   * Elemental As typically less toxic than oxides; sulfides are less acutely toxic but comparably chronically; little information available for organic arsenicals * Lung adenomas developed in inhalation study of Ca3(AsO4)2 or As2S3 (hamsters, intra-tracheally instilled, 3 mg/kg elemental As, weekly, duration unspecified) * Lung adenomas observed in inhalation study with AsO3 (hamsters, intra-tracheally instilled, 3.75–5.2 mg elemental As, weekly, duration unspecified). |
| DFG 2017 — |
| Summary of additional data:  A NOAEL for carcinogenic effects cannot be determined from available studies. Changed DNA methylation, histone modification and micro-RNA expression attributed to carcinogenic mechanism of action.  Reduction of As(V) to As(III) compounds is favoured under physiological conditions. Upon inhalation, As is distributed throughout the body by the blood; target organs are lungs, bladder, kidneys, skin and liver.  Human data:   * Case study of glass factory worker exposed to AsO3 reported vascular papilloma on skin of the hands, neck, and hollows of the elbows and knees * Linear dose-response relationship for lung cancer reported in 2/6 reviewed studies; remaining 4 studies cited lack of data on synergistic effects of smoking; co-exposures to other substances may account for supra-linear relationships * BEI of 50 µg for inorganic As and methylated metabolites in urine/L of urine (after several shifts, end of exposure or end of shift).   Animal data:   * Despite lower toxicity of GaAs, presence of As metabolites suggests it is bioavailable and therefore grouped with other As compounds. * NOAEL: 0.3 mg/m3 elemental As (mice, inhalation, no further information) as measured by immunological response * NOAEL: 4 mg/m3 elemental As (rats, inhalation, no further information) as measured by damage to lung tissue * *In vitro* assays are inconclusive as to mutagenic activity of As compounds; As(III) compounds have however generally indicated mutagenicity whereas As(V) compounds are only mutagenic at cytotoxic concentrations * Results from mutagenicity assays using methylated As metabolites are inconsistent. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2012 TWA: 0.05 mg/m3; STEL: 0.1 mg/m3 |
| Summary of additional data:   * The inhalational unit Risk (IUR) presented using absolute-risk linear model: 4.3x10‑3 per 1 µg/m3; value based on exposure data from epidemiological studies of the Montana (n=8,000) and Tacoma (n=2,000) groups also reported in ACGIH, 2001 * Noted that NIOSH reported 8–24 h exposure, on a TWA basis, at concentrations of 0.002–0.003 mg/m3 resulted in increased cancer mortality * NIOSH recommended that worker exposure should be <0.002 mg/m3 elemental As (15 min sampling period) * Well-conducted human study used to calculate minimal cancer risk from inhalational exposure to As * minimal cancer risk (4/100,000) calculated at 0.00028 mg/m3 elemental As (40 yr exposure) * Support a non-threshold mechanism of genotoxicity of the substances; available epidemiological studies do not allow derivation of a NOAEL. * Sum of inorganic As and monomethylarsonic acid and dimethylarsinic acid in urine collected at the end of the work week is the recommended method for biological monitoring of occupational exposure to elemental and soluble inorganic As compounds. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | No additional information. |
| IARC |  | 2012 | No additional information. |
| US EPA |  | 1991 | * Geometric mean for unit inhalation risk obtained from 2 data sets (Montana and Tacoma groups presented in ACGIH, 2001): 2.7x10-3 and 7.2x10-3 per µg/m3 respectively * Geometric mean of IUR: 4.3x10-3 /µg/m3 * Assumed that the increase in age-specific mortality rate of lung cancer only due to cumulative exposures. * The unit risk should not be used if the air concentration exceeds 2 µg/m3. |
| ECHA |  | 2017 | * Excess lifetime lung cancer mortality risk 0.00014 per mg/m3 elemental As (or 1.4 per µg/m3). |
| US NIOSH |  | 1994 | * IDLH based on a lowest lethal concentration (LCLo) of 100 mg/m3 for AsCl3 (cat, 1 h). |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | No |
| --- | --- |
| 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.1A |
| HCIS | Carcinogenicity – category 1A |
| NICNAS | Carc. Cat 1 |
| EU Annex | Carcinogenicity – category 1A (compounds) |
| ECHA | Carcinogenicity – category 1A |
| ACGIH | Carcinogenicity – A1 |
| DFG | Carcinogenicity –1 |
| SCOEL | NA |
| HCOTN | Carcinogenicity – category 1A |
| IARC | Carcinogenicity – Group 1 |
| US NIOSH | — |

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 data to assign a skin notation |

### IDLH

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

## Additional information

| Molecular weight: | 74.9 (elemental) |
| --- | --- |
| 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) (2002) Arsen und anorganische Arsenverbindungen (mit Ausnahme von Arsenwasserstoff) – MAK value documentation German language edition.

Deutsche Forschungsgemeinschaft (DFG) (2014) Arsenic and its inorganic compounds (with the exception of arsine) – MAK value documentation.

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European Chemicals Agency (ECHA) (2017) Committee for Risk Assessment RAC Opinion on Arsenic acid and its inorganic salts ECHA/RAC/A77-O-0000001412-86-148/F

Health Council of the Netherlands (HCOTN) (2012) Arsenic and inorganic arsenic compounds. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2012/32.

International Agency for Research on Cancer (IARC) (2012) Arsenic, Metals, Fibres and Dust. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) Arsenic: Human health tier II assessment: Human health tier II 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)

US Environmental Protection Agency (US EPA) (1991) Arsenic, inorganic – Integrated Risk Information System (IRIS) documentation.US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Arsenic (inorganic compounds, as As).