# Iron salts, soluble (as fe)

| CAS number: | — |
| --- | --- |
| Synonyms: | — |
| Chemical formula: | — |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **1 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 1 mg/m3 is recommended in the interim to protect for lung inflammation and potential local irritation in exposed workers.

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

Iron salts are used in sewage treatment, textile pigmentation, metallurgy, pharmaceuticals and as livestock feed additives.

Critical effects of exposure are lung inflammation, as observed in animals and potential local irritation.

The toxicological database for iron (II) and iron (III) salts is limited (ACGIH, 2018; HCOTN, 2004). The onset of lung inflammation and irritation are reported in a single sub-chronic inhalational study with rabbits exposed to ferric chloride (FeCl3) at a LOAEC of 1.4 mg/m3 (HCOTN, 2004). Both ACGIH (2018) and HCOTN (2004) recommend a TWA equivalent of 1 mg/m3. The basis of these recommendations is not discussed in the primary sources.

In view of the highly limited availability of toxicological data, a TWA of 1 mg/m3 is recommended in accordance with the recommendations reported in the primary sources. However, further assessment of additional data sources, regarding other iron salts and their inhalational toxicity, is recommended at the next scheduled review. Particularly, the LOAEC of 1.4 mg/m3 of FeCl3 for lung inflammation and irritation in rabbits should be examined considering its use by HCOTN (2004) to derive the proposed health‑based recommended OEL (HBROEL).

## Recommendation for notations

The assessed chemicals are not classified as carcinogens 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.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1995 TWA: 1 mg/m3 | |
|  |
| ACGIH 2001 TLV-TWA: 1 mg/m3 |
| TLV-TWA intended to minimise potential for skin and respiratory tract irritation and applies to various water-soluble iron salts.  Summary of data:  Grouped assessment of 5 model water-soluble Fe(II) and Fe(III) salts; FeCl3, Fe(NO3)3, Fe2(SO4)3, FeCl2 and FeSO4. TLV-TWA based on weight of evidence, suggests exposures below a threshold of 1 mg/m3 for dusts and aerosols is protective of irritation effects. Derivation is not reported.  Human data:   * Probable lethal dose in humans estimated at 28–473 g in a 70 kg individual * Ingestion of 3 g (Fe as tablets, salt not specified) in children led to mild poisoning; severe poisoning at 6 g (no further details provided) * Serum concentrations of >500 µg/100 mL are lethal * Lowest toxic oral dose in infants: 600 mg/kg; adverse effects to gastrointestinal tract * Adverse effects to gastric mucosa, cardiovascular/peripheral circulation and CNS (shock, coma or death) and metabolic acidosis reported at oral dose of 60 mg/kg in adult female * Overall fatality rate of 1% in 474 cases of acute iron poisonings * Inhalation of iron salt dusts and mists considered irritating to the respiratory tract, Fe(III) salts also considered skin irritants.   Animal data:   * FeCl3 and Fe(SO4)3 highly toxic by parenteral injection relative to oral doses; IP LD50 of FeCl3: 68 mg/kg (mice) compared with oral LD50: 400 mg/kg * Elemental iron much less acutely toxic than soluble iron salts (no further details provided) * No sub-chronic/chronic studies presented.   Insufficient data to recommend TLV-STEL or notations for carcinogenicity, skin absorption or sensitisation. |
| DFG NA NA |
| No report. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2004 TWA: 1 mg/m3 |
| Summary of additional data:  Grouped assessment of FeCl3, Fe(NO3)3, Fe2(SO4)3, FeCl2 and FeSO4 (same as ACGIH, 2018). Current administrative OEL considered too high, health-based recommended OEL (HBROEL) derived from LOAEL of 1.4 mg/m3 for adverse lung effects in rabbits. An overall factor of 12 is applied to account for the absence of a NOAEL, inter- and intraspecies differences, short exposure duration and the type of effect, which results in the HBROEL of 0.1 mg/m3. The agency clarifies that this HBROEL is recommended for Fe(III) salts due to the lack of data for corresponding Fe(II) salts, for which no HBROEL is currently derived.  Human data:   * Absorption of ingested iron depends on homeostatic balance, 2–15% of iron in ingested food is absorbed. * Aqueous extracts of cement containing FeSO4 did not elicit sensitisation response in volunteer patch test (n=8); volunteers were sensitive to chromate * No adverse effects to lung function in asthmatic (n=18) and non-asthmatic (n=20) volunteers exposed to 0.075 mg/m3 Fe2(SO4)3 (0.02 mg/m3 as Fe) at rest or following exercise (2 h); 5 volunteers showed small decrements in lung function, but 9 improved following exposure:   + concludes actual NOAEL for instant/acute effects on the respiratory tract are probably >0.075 mg/m3 (0.02 mg/m3 as Fe).   Animal data:   * Oral LD50 values for all assessed salts range between 400–4,500 mg/kg (mice, rats); FeCl3 is generally the most toxic * Increased lung weight, granular lung macrophages accumulation and localised interstitial inflammatory reactions at 3.1 mg/m3 FeCl3 (highest tested dose) in sub-chronic inhalation study (rabbits, n=8, 6 h/d, 5 d/wk, 2 mo); accumulation of normal alveolar macrophages and some granular ones at 1.4 mg/m3 (lowest tested dose):   + LOAEL: 1.4 mg/m3 for adverse lung effects as considered by the agency * Reduced body weight and water intake at ≈170 and ≈320 mg/kg/d in chronic feeding carcinogenicity study (rats, drinking water, 2 yr); no difference in cancer incidence compared to controls * Negative results in local lymph node assay suggest water-soluble iron salts do not cause contact dermatitis in rats, mice and guinea pigs * *In* *vitro*: FeSO4 mutagenic without metabolic activation in bacteria; equivocal results in the presence of liver cell lysates in bacteria and yeast, FeCl3 non-mutagenic with or without metabolic activation in bacteria and yeast * *In vivo*: FeCl3, but not FeSO4, induced micronuclei in stomach of fasting mice dependent on dose: 10–65 mg/kg; no micronucleus induction in normally fed mice * Clastogenicity: FeCl3 did not cause chromosomal aberrations in Chinese hamster ovarian (CHO) cells, but FeSO4 did. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | FeCl3:   * LD50: >2,000 mg/kg (rabbits, dermal) * No data on genotoxicity or carcinogenicity available, but no systemic toxicity is expected at low concentrations. |
| ECHA |  | 2019 | * Considered low inhalation hazard, no threshold limit derived * No human genotoxicity data available * All relevant animal studies indicate substances are non-genotoxic; 2 insufficiently documented chromosomal aberration studies report positive results, but not considered in the agency’s assessment * Generally, most data support non-genotoxic conclusion. |

### 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 | FeCl3 and FeSO4: —  All other salts: NA |
| NICNAS | FeCl3: —  All other salts: NA |
| EU Annex | FeSO4: —  All other salts: NA |
| ECHA | — |
| ACGIH | — |
| DFG | NA |
| 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

| Calculation |
| --- |
| Insufficient data to assign a skin notation |

### IDLH

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

## Additional information

| Molecular weight: | Varies |
| --- | --- |
| 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.

European Chemicals Agency (ECHA) (2019) Diiron tris(sulphate) – REACH assessment.

European Chemicals Agency (ECHA) (2019) Iron dichloride – REACH assessment.

European Chemicals Agency (ECHA) (2019) Iron sulphate – REACH assessment.

European Chemicals Agency (ECHA) (2019) Iron trichloride – REACH assessment.

European Chemicals Agency (ECHA) (2019) Iron trinitrate – REACH assessment.

Health Council of the Netherlands (HCOTN) (2004) Iron salts, water-soluble. Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/102.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Iron chloride and its hydrates: 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).