# Iron oxide fume and DUST (FE2O3) (as Fe)

| CAS number: | 1309-37-1 |
| --- | --- |
| Synonyms: | Ferric oxide, haematite, burnt umber, rouge dust |
| Chemical formula: | Fe2O3 |

Workplace exposure standard (interim)

| TWA: | **5 mg/m3 (as Fe, respirable particulate fraction)** |
| --- | --- |
| 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

An interim TWA of 5 mg/m3 for respirable particulate matter is recommended to protect for lung inflammation and pulmonary siderosis in exposed workers.

A priority review of the data for the chemical in the next scheduled review of the workplace exposure standards is recommended.

## Discussion and conclusions

Iron oxide is used as a polish, a pigment, a component of cement and as a catalyst. It is also used in electronics and may be present in welding fumes.

Critical effects of exposure are inflammatory responses in the lungs and pulmonary siderosis. Findings of the available epidemiological data are frequently confounded by mixed exposures to silica, diesel exhaust, radioactive materials in mining-related exposures or other metals in studies of welding fume exposures. Chronic inhalation above 10 mg/m3 is associated with the development of a benign form of pulmonary siderosis that produces radiographic changes in the lungs of exposed workers (ACGIH, 2018). A retrospective cohort study showed that elimination of such co-exposures at a mining site did not lead to excess lung cancers (ACGIH, 2018). Experimental human and animal data provide evidence for inflammatory reactions in the lungs, which may be elicited by responses to both mechanical and chemical toxicity (ACGIH, 2018; DFG, 2011). At high repeated intratracheal doses in animals, these inflammatory responses have been associated with tumorigenicity (DFG, 2011). However, it is unclear if residual solubility of deposited inhaled particulate matter is sufficient to induce oxidative stress in exposed tissue.

An interim TWA of 5 mg/m3 is recommended as it is expected to protect for inflammatory responses identified in human and animal experiments, and is lower than the concentrations reported in cases of chronic pulmonary siderosis in workers. A prioritised review of the available carcinogenicity data, and therefore the suitability of the interim TWA, is recommended during subsequent assessments.

## 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.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 mg/m3 | |
|  |
| ACGIH 2006 TLV-TWA: 5 mg/m3 (respirable particulate fraction) |
| TLV-TWA is intended to protect for non-specific inflammatory responses and radiographic lung changes from chronic exposures.  Summary of data:  Chronic exposures lead to clinically benign pulmonary siderosis. The substance alone does not cause fibrotic changes, but causes mild inflammatory responses in the lungs. TLV-TWA based on weight of evidence that siderosis occurs between 10–700 mg/m3 in humans, and the onset of inflammatory responses occurs near 20 mg/m3 in animals.  Human data:   * Transient alveolar inflammation in BAL fluid at 5 mg instilled in lungs of volunteers (n=36), inflammatory response likely due to residual solubility of iron * Concomitant exposure to radon associated with increased carcinogenicity * Radiographic changes in lungs of welders not associated with any adverse clinical effects in several case studies (exposure concentrations and durations not specified)   + welders exposed to mixtures of welding fumes (primarily Fe2O3) at 1–294 mg/m3 developed siderosis, study concluded that Fe2O3 exposure does not lead to fibrotic pulmonary changes. * Co-exposures to silica, radon or diesel exhaust e.g. in haematite mining, or exposure to freshly formed substance may lead to pneumoconiosis and fibrotic changes in lungs;   + chronic (6–10 yr) exposure to Fe2O3 alone caused Fe deposition (siderosis) and produces radiographic changes in the lungs without adverse clinical effects * Several epidemiological studies support a conclusion that exposure is not causal in development of chronic adverse effects, but confounding factors such as mixed exposures, e.g. to general welding fumes, complicate the use of some studies in the agency’s evaluation. * Deficits in mortality and no excess of lung cancer reported in retrospective cohort study (n=10,403) of haematite miners in a US mine with good occupational hygiene practices; i.e. no diesel exhausts, low co-exposure to radon and silica and non-smoking workplace.   Animal data:   * No evidence for irreversible lung damage, but inflammatory response noted, from single or repeat intratracheal instillations of 3 mg (hamsters) or 50 mg (guinea pigs)   + particles rapidly cleared by mucociliary action * Transient inflammatory responses at 274 mg/m3 (hamsters, rabbits, 2 h)   + no significant changes in concentrations of inflammatory response cells in lung lavage at 20 mg/m3 (2 h), but increased phagocytic activity observed * No evidence for carcinogenicity in several chronic inhalation and intratracheal instillation studies (mice, hamsters, and guinea pigs, concentrations and duration not specified)   + no carcinogenicity, chronic inflammation or necrosis observed when substance used as a vehicle control in chronic studies with known carcinogens   + increases metabolism of B(a)P, which forms more carcinogenic metabolites in the presence of iron oxide   + injection of high concentrations (not specified) caused increased incidence of sarcomas at injection site, but considered irrelevant to occupational exposure.   Negative results for carcinogenicity in animal experiments suggest the substance is not carcinogenic.  Insufficient data available to assign a TLV-STEL or notation for skin absorption.  A sensitiser notation is not warranted due to low incidence of sensitisation in human studies. |
| DFG 2011 Not assigned |
| Summary of additional information:  MAK evaluated for particles in inhalable fraction and as grouped assessment of Fe(II), Fe(III), and mixed oxides. MAK not established due to potential for genotoxic carcinogenicity caused by generation of ROS associated with excess soluble Fe ions above homeostatic levels. It is unclear if endogenous Fe elimination pathways are sufficient to prevent the formation of free Fe ions and no NOAEL is reported for this effect; a MAK can therefore not be derived.  Sensitiser notation not warranted due to rare occurrence of contact dermatitis in humans, positive results in these tests are attributed to Ni impurities and non-specific reactions to the test formulation.  Human data:   * Epidemiological studies regarding co-exposures, e.g. to B(a)P and silica, not considered in agency’s evaluation due to confounding co-exposures * Large epidemiological studies (no details provided) indicate high oral iron intake and high Fe storage levels are associated with increased tumorigenicity due to increased potential for oxidative stress; Fe is also a limiting nutrient in proliferative cell growth * No effects on blood and urine parameters, blood pressure or signs of intolerance in oral and iv infusion volunteer studies; no effects on lung function at 12.7 mg/m3 in inhalational study (n=16, 30 min) * Oedema reported in 1/62 patients treated with an Fe2O3-containing formulation for treatment of scar pigmentation on scalp * Positive sensitisation after 3 d in 6/126 and 1/64 patients in patch test with 2% Fe2O3.   Animal data:   * Non-irritating to eyes (rabbits), mechanical effects caused irritation in eyes of rats * Elevated concentrations of inflammatory response indicators in BAL fluid at ~200 mg/m3 (2 wk) or 10 mg/m3 (4 wk) 4.7 mg/m3 (90 d) of different Fe2O3 morphologies (rats, 6 h/d, 5 d/wk, 2, 4 wk, or 90 d); responses reversed within 107–197 d observation period   + comparison to TiO2 (poorly soluble particle) suggests inflammatory response may be due to particle/clearance overload and greater particle surface area rather than inherent chemical toxicity of Fe2O3 * Increased incidence of lung tumours in chronic intratracheal instillation studies at   15–150 mg in saline (rats, 15 doses, 2–2.5 yr);   * + no increased tumour incidence with hamsters chronically exposed up to 50 mg by intratracheal instillation   Non-genotoxic in bacteria *in vitro*, but induced DNA repair in combination with B(a)P *in vivo*. |
| 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 |
| --- | --- | --- | --- |
| NICNAS |  | 2018 | * Tier I assessment: Chemical identified as low concern to human health by application of expert validated rules. |
| IARC |  | 1972 | * Survey of literature does not indicate elevated risk of lung cancer in exposed welders (n=300); unlikely Fe2O3 is solely responsible for diseases reported in exposed welders * Non-carcinogenic in animals given intratracheal instillations * Haematite dust may increase the risk of lung cancer development in underground workers but not surface workers, possibly due to confounders such as airborne silica or radioactive dust. |
| ECHA |  | 2019 | * Grouped assessment of Fe(II) and Fe(III) oxides; NOAEC of 4.7 mg/m3 Fe3O4 for increased inflammatory response markers in BAL fluid in inhalational studies used to support DNEL (cited by DFG, 2011) * Grouped substances treated as dust without specific toxicity;, DFG general dust limit for respirable particles adopted as recommended OEL (3 mg/m3); NOAEC of 4.7 mg/m3 is higher than the respirable dust limit * Non-specific toxicity consistent with a ‘poorly soluble particle’ and no specific toxicity observed at higher concentrations * No evidence of systemic toxicity, genotoxicity or carcinogenicity. |
| US NIOSH |  | 1994 | * IDLH for Fe2O3 dust and fume is 2,500 mg/m3 based on being 500 times the NIOSH REL of 5 mg/m3 * Value not adopted due to lack of experimental basis. |

### 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 | NA |
| NICNAS | — |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4 |
| DFG | Carcinogenicity – 3B |
| SCOEL | NA |
| HCOTN | NA |
| IARC | — |
| 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: | 177.7 |
| --- | --- |
| 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) (2011) Iron oxides (inhalable fraction) – MAK value documentation.

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

International Agency for Research on Cancer (IARC) (1972) Some Inorganic Substances, Chlorinated Hydrocarbons, Aromatic Amines, N-Nitroso Compounds, and Natural Products. IARC Monographs, volume 1.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Iron oxide (Fe2O3): Human health tier I assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Iron oxide dust and fume (as Fe).