# Nickel, Soluble Compounds

| CAS number: | 7718-54-9 (Nickel dichloride)  13138-45-9 (Nickel dinitrate) |
| --- | --- |
| Synonyms: | Nickel, soluble compounds (as Ni), nickel salt (nitric acid) |
| Chemical formula: | Ni |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **0.1 mg/m3 (Ni, inhalable)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1A; DSEN; RSEN** |
| IDLH: | **10 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 0.1 mg/m3 (Ni, inhalable) is recommended to protect for pulmonary damage and possible carcinogenic effects in the respiratory system in exposed workers.

## Discussion and conclusions

Nickel has been used in the production of stainless steel, corrosion and heat resistant alloys, catalysts for hydrogenation of fats and oils, electroplating, coinage and alkaline (NiCad) batteries.

This evaluation covers soluble nickel compounds including nickel dichloride, nickel dinitrate, nickel sulfate and soluble nickel salts.

The critical effect of exposure is respiratory cancer.

Several agencies have classified nickel compounds as carcinogenic, causing cancer in the lungs and nasal cavity based on observational studies in workers (DFG, 2010; NICNAS, 2014; SCOEL, 2011). The available evidence suggests respiratory cancer risks in nickel refinery workers is primarily related to exposures to soluble nickel compounds of greater than 1 mg/m3 (ACGIH, 2018). Excess of bronchial cancer and two cancers of the nasal cavity among workers exposed at concentrations of approximately 0.25 mg/m3 water soluble nickel salts were reported in an epidemiological study. A significant increase in cancer incidence for water soluble nickel in workers was observed at a cumulative exposure of 1.6 mg/m³ x years, which was reported to be equivalent to 0.04 mg/m³ (Ni) when calculated for 40-year exposure (SCOEL, 2011). AIOH (2016) reported the 0.04 mg/m3 (Ni) as 0.1 mg/mg3 measured as the inhalable fraction and recommends this concentration as a TWA OEL.

Inhalation of soluble nickel concentrations high enough to induce chronic lung inflammation may enhance carcinogenic risks. No respiratory cancers in rats (0.11 mg/m3) and mice (0.22 mg/m3) were reported in a two-year inhalation study with nickel sulfate. From this study, a NOAEL of 0.12 mg/m3 (nickel sulfate) was identified in rats for inflammation related reactions, which was reported as equivalent threshold value of 0.01 mg/m3 in humans (DFG, 2010). Pulmonary damage was reported in animals exposed at 0.1 to 1.0 mg/m3 total aerosol (ACGIH, 2018). Readily soluble nickel salts accumulate in the lung to a lesser degree than poorly soluble compounds. Nickel and nickel compounds are not directly mutagenic and carcinogenicity is due to other mechanisms (AIOH, 2016; DFG, 2010; SCOEL, 2011). As such, soluble nickel compounds are considered to have a carcinogenicity threshold.

The current SWA TWA of 0.1 mg/m3 is recommended be retained to protect for pulmonary damage and possible carcinogenic effects in the respiratory system in exposed workers. This TWA aligns with ACGIH (2018).

## Recommendation for notations

Classified as a category 1A carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and 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: 0.1 mg/m3 (Nickel, soluble compounds (as Ni)) | |
| Adopted in 1991 from ACGIH |
| ACGIH 2001 TLV-TWA (inhalable nickel particulate mass): 0.1 mg/m3(Ni) (soluble compounds) |
| TLV-TWA recommended to minimise the potential for pulmonary damage, as well as dermatitis and suspected cancer risk.  Summary of data:   * Soluble compounds identified in review: * Nickel chloride 7718-54-9 * Nickel sulfate 10101-97-0 * Nickel nitrate 13478-60-7 * Nickel sulfamate 13770-89-3 * Nickel ammonium chloride 16122-03-5 * Nickel acetate 6018-89-9 * Monitoring data based primarily on “total” nickel particulate; recommends concentrations should expressed in terms of inhalable nickel particulate not total * TLV-TWA based primarily of 1 mg/m3 thresholdin humans for cancer supported by evidence of pulmonary damage in animals exposed at 0.1–1.0 mg/m3 “total” aerosol (soluble and insoluble).   Human data:   * Refers to extensive review ‘*International Committee on Nickel Carcinogenicity in* *Man’* reporting the following: * exposures to soluble nickel increased the risk of lung and sinus cancer; may have enhanced the risk of exposure to less soluble forms * available evidence suggests respiratory cancer risks in nickel refinery workers is primarily related to exposures >1 mg/m3 (soluble nickel compounds) * no evidence of increased risk of other forms of cancer.   Animal data:   * Rats and mice exposed at 0.7­–13.5 mg/m3 (nickel sulfate hexahydrate as Ni) 6 h/d for 12 d; pulmonary inflammation, degeneration of bronchiolar mucosa and atrophy of olfactory epithelium at all concentrations; effects greater in rats * Rabbits exposed to nickel chloride at 0.3 mg/m3 (Ni) 6 h/d, 5 d/wk for 1 mo; increase in the number and volume of alveolar epithelial cells, nodular accumulation of macrophages and laminated structures and an increase in phospholipids in lower lobes of the lungs * Rats exposed (2 yr) to nickel sulfate at 0, 0.12, 0.25 or 0.5 mg/m3 (0, 0.03, 0.06 or 0.11 mg/m3 (Ni)); mice at 0, 0.25, 0.5 and 1.0 mg/m3 (equivalent to 0, 0.06, 0.11 or 0.22 mg/m3 (Ni)) * rats exposed at 0.06 and 0.11 mg/m3 (Ni); chronic, active pulmonary inflammation; macrophage hyperplasia; alveolar proteinosis; fibrosis; hyperplasia of the bronchial lymph nodes; and atrophy of the olfactory epithelium * mice exposed at 0.11 and 0.22 mg/m3 (Ni); similar inflammatory changes as rats * no evidence of any carcinogenic effects * No genotoxicity was found in *in vivo* studies. |
| DFG 2010 Not assigned |
| Reviewed as a group ‘Nickel and its compounds (in the form of inhalable dusts/aerosols)’.  Summary of data:   * Soluble nickel salts, such as nickel sulphate, nickel chloride, nickel acetate and comparable nickel compounds, are classified in Carcinogenicity category 1 * Carcinogenicity of nickel compounds is probably due to mechanisms that are not directly genotoxic: * mutagenicity is only weak and mechanistic studies have shown an inhibition of DNA repair and a stimulation of cell proliferation.   Human data:   * Study of workers at electrolytic nickel refining factory 1916–1983; 1,979 mortalities; mean exposure concentrations: * 0.1 mg/m3, 86 cases of lung cancer; RR 1.0; reference * 2.3 mg/m3, 36 cases, RR 1.2 * 8.8 mg/m3, 23 cases, RR 1.6 * 28.9 mg/m3, 55 cases, RR 3.1 * Increase in cancer incidence in a cohort of 369 nickel refining workers with a total of 8,794 person years; significant increase in risk of nasal cancer positively associated with latency and duration of employment * No increased lung cancer mortality was found in a cohort of 284 nickel platers employed from 1945–1975; validity of this study is questionable.   Animal data:   * 2-yr inhalation study with nickel sulfate * no respiratory cancers in rats (0.11 mg/m3) and mice (0.22 mgm3) * rats exposed at ≥0.06 mg/m3 (Ni) demonstrated chronic, active pneumonia, hyperplasia of the macrophages, alveolar proteinosis, fibrosis, hyperplasia of the bronchial lymph nodes and atrophy of the olfactory epithelium * mice exposed at ≥0.06 mg/m3 (Ni) demonstrated similar inflammatory responses * NOAEL of 0.03 mg/m3 (Ni) or 0.12 mg/m3 (nickel sulfate) in rats * NOAEL of 0.06 mg/m3 (Ni) or 0.25 mg/m3 (nickel sulfate) in mice.   Using the lowest NOAEL (NOAEC) a threshold value for inflammatory reactions of the lungs of about 0.01 mg/m3 (Ni) would be obtained for humans; no derivation provided. |
| SCOEL 2011 TWA: 0.01 mg/m3 (inhalable fraction of water soluble as well as poorly water soluble nickel compounds, excluding metallic nickel), 0.005 mg/m3 (respirable fraction) |
| TWA to protect for inflammatory effects in the lung. Available evidence also indicates protection for nickel-induced carcinogenicity; reviewed nickel and its soluble and insoluble compounds.  Summary of additional data:   * Readily soluble nickel salts are not accumulated in the lung as much as the poorly soluble oxides and sulphide * In rats, ≈98% water soluble nickel or 6% metallic nickel were bioavailable after inhalation; no further information * Carcinogenicity evaluated on same studies evaluated by DFG (2010); no cohorts available exclusively exposed to a single nickel species * Nickel and nickel compounds are not directly mutagenic; at low concentrations nickel ions do not directly interact with DNA but rather exert indirect genotoxic effects * SCOEL reports that the ‘*International Committee on Nickel Carcinogenicity in Man’* concluded that the increase in cancers of the nasal cavity and lungs among workers in nickel refineries is associated with a minimum exposure of 1 mg/m3 for water soluble salts; no further information * SCOEL reports an excess of bronchial cancer and two cancers of the sinuses (nasal cavity) among workers exposed at concentrations of about 0.25 mg/m3 water soluble nickel salts (sulphate) in a Finnish epidemiological study * A significant increase in cancer incidence for water soluble nickel was observed at a cumulative exposure of 1.6 mg/m³ x years, equivalent to 0.04 mg/m³ (Ni) when calculated for 40 yr exposure; basis for OEL. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2003 Not assigned |
| Review of developmental and reproductive effects. |

### Secondary source reports relied upon

| **Source** |  | **Year** | **Additional information** |
| --- | --- | --- | --- |
| AIOH |  | 2016 | * No excess respiratory cancer in a cohort of Canadian electrolysis workers exposed exclusively to soluble nickel showed * Considers uncertainty regarding carcinogenicity of soluble nickel compounds; however, inhalation of soluble nickel concentrations high enough to induce chronic lung inflammation that may enhance carcinogenic risks associated with inhalation exposure to other substances; no further information * Considers respiratory cancer (lung and nasal) as the main health effect to be protected by an OEL * Calculates that adjustment of the 0.04 mg/m3 concentration reported by SCOEL (2011) is equivalent to 0.1 mg/m3 as the inhalable fraction * Clear evidence of nasal and lung cancer in a study of 2,521 refinery workers with more than 5 yr employment between 1902 and 1969 at relatively high exposures to airborne nickel: * follow up studies with greatly reduced exposures provided limited evidence of elevated lung cancer risks associated with exposures at <0.2 mg/m3 total nickel * Recommends a TWA for nickel (including both readily soluble and sparingly soluble (insoluble) compounds) at 0.1 mg/m3 (inhalable aerosol fraction) * The occurrence of multiple species in most work environments and the difficulty in speciation suggest a common limit for all species. |
| NICNAS |  | 2014 | * Human health tier II assessment of group defined as soluble nickel chemicals: nickel fluoride, nickel nitrate and their respective tetrahydrate and hexahydrate salts * No specific inhalation data available; assessments of nickel sulfate and nickel chloride can be read-across to chemicals of this group given that the chemicals in this group have similar bioaccessibility and bioavailability to nickel sulfate * Critical effects considered to be systemic long-term effects; local carcinogenic long term effects; systemic and local acute effects. |
| NICNAS |  | 2014 | * Human health tier II assessment of nickel metal including some evidence about soluble compounds * Case-control study conducted in a cohort of nickel-refinery workers showed a clear dose-related effect for soluble nickel and lung cancer; exposure to metallic nickel was reported to be correlated (r = 0.71) with soluble nickel compounds; indicated exposure to nickel metal and soluble nickel compounds together associated with the incidence of lung cancer; no further information. |

### 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 | Carcinogenicity – category 1A, Skin sensitisation – category 1, Respiratory sensitisation – category 1 |
| NICNAS | Carc. Cat. 1 |
| EU Annex | Carcinogenicity – category 1A, Skin sensitisation – category 1, Respiratory sensitisation – category 1 |
| ECHA | Carcinogenicity – category 1A |
| ACGIH | Carcinogenicity – A4 (Soluble inorganic compounds) |
| DFG | Carcinogenicity – 1, Sh (dermal sensitiser), Sa (respiratory sensitiser) |
| SCOEL | Carcinogenicity – C (excluding metallic nickel) |
| HCOTN | — |
| IARC | Group 1 |
| 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. |

### IDLH

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

## Additional information

| Molecular weight: | 129.61 (Nickel dichloride)  182.72 (Nickel dinitrate) |
| --- | --- |
| 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 Institute of Occupational Hygienists (AIOH) Australian Institute of Occupational Hygienists (AIOH) (2016) Position paper Nickel and its compounds – potential for occupational health issues.

Deutsche Forschungsgemeinschaft (DFG) (2006) Nickel and its compounds (in the form of inhalable dusts/aerosols) – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2011) Recommendation from the Scientific Committee on Occupational Exposure Limits for nickel and inorganic nickel. SCOEL/SUM/85.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Health Council of the Netherlands (HCOTN) (2003) Nickel and its compounds. Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands; publication no. 2003/05OSH.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Nickel chloride: Human health tier II assessment – IMAP report.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Nickel nitrate and nickel fluoride: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU) 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 National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – nickel metal and other compounds (as Ni).