Nickel: Human health tier II assessment

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- Preface
- Chemical Identity
- Import, Manufacture and Use
- Restrictions
- Existing Work Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

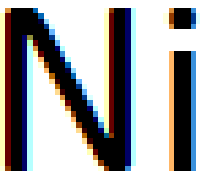
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Nickel metal
Structural Formula	
Molecular Formula	Ni
Molecular Weight (g/mol)	58.7
Appearance and Odour (where available)	Odourless silver - white solid metal.
SMILES	[Ni]

Import, Manufacture and Use

Australian

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information was greater than 10000 tonnes.

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information:

The chemical has reported commercial use including:

- as a commercial material additive;
- in electroplating;
- as an insulating agent; and
- as a welding and soldering agent.

The chemical has reported site-limited use including:

- in manufacturing stainless steel and alloys;
- in manufacturing welding electrodes;
- in manufacturing flux cored wire;
- as a catalyst; and
- as an ingredient in mineral oil lubricant.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported domestic use including in:

- automotive products; and
- home maintenance products.

The chemical has reported commercial use including:

- as a construction material additive;
- as a welding and soldering agent;
- in electroplating;
- in insulation;
- in paints, lacquers and varnishes;
- in corrosion inhibitors;
- as a colouring agent; and
- in absorbents, adsorbents, adhesives and binding agents

The chemical has reported site-limited use including:

- in manufacturing stainless steel and alloy steels;
- in manufacturing non-ferrous alloys;
- in manufacturing flux agents or joining materials;
- in manufacturing magnets;
- as an analytical reagent;
- in electroplating;
- as a catalyst; and
- in manufacturing nickel based batteries.

Restrictions

Australian

Nickel and its compounds are listed in Schedule 10 (prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals) of the Work Health and Safety Regulations for restricted use in abrasive blasting at a concentration of greater than 0.1 % of nickel (WHS, 2011).

International

REACH Regulations Annex XVII Section 27 on nickel and its compounds states:

'1. Shall not be used:

(a) in all post assemblies which are inserted into pierced ears and other pierced parts of the human body unless the rate of nickel release from such post assemblies is less than 0.2 $\mu g/cm^2$/week (migration limit);

(b) in articles intended to come into direct and prolonged contact with the skin such as:

- earrings,
- necklaces, bracelets and chains, anklets, finger rings,
- wrist-watch cases, watch straps and tighteners,
- rivet buttons, tighteners, rivets, zippers and metal marks, when these are used in garments,
- if the rate of nickel release from the parts of these articles coming into direct and prolonged contact with the skin is greater than 0.5 $\mu g/cm^2$/week;

(c) in articles such as those listed in point (b) where these have a non-nickel coating unless such coating is sufficient to ensure that the rate of nickel released from those parts of such articles coming into direct and prolonged contact with the skin will not exceed 0.5 $\mu g/cm^2$/week for a period of at least two years of normal use of the article.

2. Articles which are the subject of paragraph 1, shall not be placed on the market unless they conform to the requirements set out in those points.

3. The standards adopted by the European Committee for Standardisation (CEN) shall be used as the test methods for demonstrating the conformity of articles to paragraphs 1 and 2' (REACH Annex XVII, 2009).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

R43 (Skin sensitisation);

R48/23 (Repeated dose toxicity); and

Carc. Cat. 3; R40 (Carcinogenicity).

Exposure Standards

Australian

The chemical has an exposure standard of 1 mg/m^3 time weighted average (TWA) (HSIS).

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit of 0.015–1.5 mg/m^3 time weighted average (TWA) in different countries such as USA (Alaska, Hawaii—1 mg/m^3), Canada (Alberta—1.5 mg/m^3), Norway (0.05 mg/m^3) and Switzerland (0.05 mg/m^3).

Health Hazard Information

Toxicokinetics

Nickel can be absorbed via inhalation, ingestion and, to a limited extent, following dermal exposure. Nickel is metabolised extracellularly through a series of ligand exchange reactions and binds albumin proteins in the blood consistently across humans, rats and bovine species (ATSDR, 2005; EU RAR, 2008). With respect to nickel metal specifically, absorption occurs in the form of the Ni^{2+} ion which may be released from surface oxidation of nickel metal or acid digestion (EU RAR, 2008).

Inhalation exposure

Data available from two chronic inhalation studies (28-day and 13-week) showed that nickel lung burden and blood nickel concentrations increase with increasing exposure concentration. Data from the 13-week inhalation study indicated that no more than 6 % of the inhaled dose was absorbed (EU RAR, 2008).

Oral exposure

In a study conducted in male Wistar rats administered a single oral dose of 10 mg of nickel metal in a 5 % starch saline solution, absorption was estimated to be 0.09 %, which indicates 100 fold lower absorption of nickel following administration of nickel metal than for soluble nickel compounds. The chemical was distributed in significantly increased quantities in the lungs, kidneys and pancreas, and almost completely excreted 24 hours after administration (REACH). A further oral administration study using Raney nickel (4–6 μm particle size) showed that peak nickel concentrations in the blood occurred six hours after administration (EU RAR, 2008).

Dermal exposure

A study conducted in human volunteers examined the surface distribution of nickel powder (25 mg, 3 μm particle size) on forearm skin following occlusive application. A tape-stripping method showed that nickel metal in contact with human skin could be oxidised to a form that was diffusible through the stratum corneum, and that nickel metal was able to penetrate the stratum corneum and reach the viable epidermal layer. The researchers estimated that the majority of the nickel metal was left on the skin and a minor amount (0.2 %) was absorbed (EU RAR, 2008).

Acute Toxicity

Oral

The chemical had low acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in Sprague Dawley (SD) rats is greater than 9000 mg/kg bw. Observed sub-lethal effects included diarrhoea in the highest dose group of 9000 mg/kg bw (REACH).

Dermal

No data are available.

Inhalation

There are no available guideline acute toxicity studies via the inhalation route. However, the chemical had low acute toxicity following acute inhalation exposure with a no observed adverse effect concentration (NOAEC) of ≥10.2 mg/L (REACH).

In a non-guideline study, 10 male and 10 female SD rats were exposed to 10.2 mg/L nickel powder for one hour, and observed for 14 days following exposure. No signs of toxicity were seen throughout the observation period (EU RAR, 2008; REACH). The NOAEC was ≥10.2 mg/L (REACH).

In a second study, male Wistar rats were exposed to a single intratracheal administration of either standard nickel powder (ST—5 μm diameter) or fine nickel powder (FN—20 nm diameter) at 0, 0.1, 0.5, 1 or 5 mg. Three days after administration, the animals were euthanised and lung weights and broncheoalveolar lavage fluid (BALF) assessed for inflammatory markers (neutrophils and lactate dehydrogenase (LDH) activity). For both forms of nickel, there was a dose-dependent increase in lung weight. However, animals administered FN—nickel showed a significantly greater number of neutrophils in BALF, and a significant increase in LDH activity compared with ST—nickel, indicating that FN—nickel induced a more severe form of pulmonary inflammation (Zhang et al., 2003).

Observation in humans

Symptoms of nausea, vomiting, weakness, headache and palpitations were reported in 23 patients after exposure to nickel during haemodialysis from a nickel-plated steel heating tank. Symptoms were observed at a plasma nickel concentration of 3 mg/L of nickel and resolved on stopping dialysis treatment (EU RAR, 2008).

A case report describes a fatal incident in a worker exposed by inhalation to an estimated concentration of 382 mg/m^3 of nickel. The worker developed pneumonia and died 13 days after exposure (EU RAR, 2008).

Corrosion / Irritation

Skin Irritation

The chemical is reported to slightly irritate skin in animal studies. The effects are not sufficient to warrant a hazard classification.

In a study conducted according to OECD Test Guideline (TG) 404, male New Zealand White rabbits were exposed to 0.5 g of nickel powder for four hours under semiocclusive conditions. The study reported mild dermal irritation at 24 and 48 hours after exposure, which completely resolved at 72 hours (REACH).

Eye Irritation

No data are available for this chemical.

The Nickel Producers Environmental Research Association (NiPERA) has indicated that based on the physical and mechanical properties of metallic nickel powders, they should be labelled as an eye irritant. In the absence of data, the European classification, labelling and packaging of substances and mixtures (EU CLP) has included a safety phrase (S—Phrase) for S39; 'Wear eye/face protection' (EU RAR, 2008).

Sensitisation

Skin Sensitisation

The chemical is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (Xi; R43) in HSIS (Safe Work Australia). No animal data are available. The available human data indicate that nickel is known to induce sensitisation, especially in those with pre-existing conditions such as eczema.

No human data are specifically available for nickel metal. Studies and/or case reports have largely reported on the nickel released from articles of nickel alloys (coins, jewellery, watches, etc.) resulting in sensitisation. In a study designed to assess nickel release in 11 widely used nickel alloys, nickel alloys that released 1 μg/cm^2/week in artificial sweat produced a strong patch test reaction in nickel-sensitive individuals. Alloys with a release rate below 0.5 μg/cm^2/week showed weak reactivity (EU RAR, 2008).

Bioaccessibility studies conducted in artificial sweat have shown that low levels of the Ni^{2+} ion (1–2.2 % of nickel) are released from nickel powder (sample ID N36 and N13 respectively) (Mazinanian et al., 2013). Given the known sensitising potential of the Ni^{2+} ion, there is the possibility that long-term exposure may cause allergic reactions (EU RAR, 2008). Therefore, in the absence of more comprehensive information, there are inadequate data to amend the classification.

Repeated Dose Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

The chemical is classified as hazardous with the risk phrase 'Toxic: danger of serious damage to health by prolonged exposure through inhalation' (T; R48/23) in HSIS (Safe Work Australia). The available data support this classification.

Three main repeated dose studies (28-day, 90-day and two-year) are described below.

In a study conducted according to OECD TG 412, male and female Wistar rats were exposed to metallic nickel (4, 8 or 24 mg/m^3 with a particle size of 1.5, 1.8 and 1.6 μm, respectively) for six hours a day, five days a week, for 28 days. Adverse effects included significantly lower body weights at the highest exposure dose (24 mg/m^3) in males compared with control animals. This coincided with significantly reduced food consumption. On necropsy, macroscopic examination of animals exposed to all three concentrations showed white and dark red areas in the lungs, incomplete collapse of the lungs and enlarged and/or discoloured lymph nodes of the mediastinal and tracheobronchial areas. Assessment of organ weights showed a significant increase in the lung weights of all animals exposed to nickel metal. Microscopic examination of the lungs showed concentration-related granulomatous inflammation, proteinaceous and/or mucoid exudate and black pigmentation of the lungs. Also, microscopic examination of the mediastinal and tracheobronchial lymph nodes showed hyperplasia and black pigmentation. A lowest observed adverse effect concentration (LOAEC) for lung inflammation was determined to be 4 mg/m^3 (REACH, EU RAR, 2008).

In a 90-day study carried out according to OECD TG 413, male and female Wistar rats were exposed to metallic nickel powder (1, 4 or 8 mg/m^3 with a particle size of approximately 1.7, 2.7 or 2.4 μm, respectively for six hours a day, five days a week, for 90 days, followed by a 90-day recovery period. Several (numbers not specified) animals were found dead or had to be euthanised in the high dose group (8 mg/m^3). Signs of clinical toxicity observed during the study included laboured respiration, hypothermia, extreme weight loss, dehydration, tremors, abnormal stools and discoloured fur and skin. Males in the 4 and 8 mg/m^3 and females in the 8 mg/m^3 groups had significant weight reduction (13, 24 and 9 %, respectively) and a correlating decrease in food consumption and weight gain as assessed at the end of the 90-day exposure phase. Following a 90-day recovery phase, mean body weights were still reduced in males and females exposed to 8 mg/m^3 (14 % and 5 %, respectively). Also, levels of haemoglobin and haematocrit were increased in males exposed to 4 and 8 mg/m^3 and females in the 8 mg/m^3 group. Following the 90-day recovery phase, changes in haemoglobin and haematocrit were still elevated in males and females exposed to 8 mg/m^3. Also, elevated neutrophil counts (correlated with lung inflammation) were recorded in males and females exposed to 8 mg/m^3 nickel at the 13- and 26-week evaluation points. Analysis of broncheoalveolar lavage fluid (BALF) at the end of the 13-week exposure period showed an exposure-dependent increase in protein and lactate dehydrogenase (LDH) levels, consistent with the severity of proteinosis observed microscopically. Further examination showed black pigmentation in the lungs, alveolar proteinosis, granulomatous inflammation, mucoid exudate, mononuclear infiltrate and fibrosis. These effects were observed with low incidence at 1 mg/m^3 but were significant at doses $\geq$4 mg/m^3 (REACH; Oller et al., 2008).

In a two-year study carried out according to OECD TG 451, male and female Wistar rats were exposed to metallic nickel powder (0, 0.1, 0.4 or 1 mg/m^3) with a mass median aerodynamic diameter (MMAD) of 1.8 μm and a geometric standard deviation of 2.4 μm, for six hours a day, five days a week, for two years, followed by a six-month non-exposure period. Excessive mortality between weeks 40 and 53 of the study in males and females exposed to 1 mg/m^3 resulted in early termination of this exposure group. Also, due to high mortality in females exposed to 0.4 mg/m^3 nickel, exposure was stopped at 19 months. Laboured breathing and cyanosis of the extremities and facial area were reported in male and female rats in the 0.4 and 1 mg/m^3 exposure group. Further effects observed at $\geq$0.1 mg/m^3 included cold/pale extremities, dermal atonia, decreased defaecation

and laboured respiration. Mean body weights were significantly reduced in males and females exposed to 0.4 mg/m^3 (27 % and 18 %, respectively) and in males only in the 0.1 mg/m^3 exposure group (11 %). Food consumption was generally correlated with effects on body weight gain. Haematological evaluation conducted after 18 weeks of exposure showed significantly elevated mean red blood cell counts, haemoglobin levels and haematocrit in males (0.1 and 0.4 mg/m^3) and females (0.4 mg/m^3). Haematological markers improved during the six-month recovery phase as noted by a change to non-significant when compared with control animals. Gross pathology showed exposure-related mottled lungs and increased lung weights in both genders, enlarged spleens in females and enlarged adrenal glands in males. Histopathology studies reported a granular brown pigment in the kidneys, extramedullary haematopoiesis in the spleen and hypercellularity of the sternum and femoral bones. Histopathology of the respiratory tract showed lung lesions of alveolar proteinosis, alveolar histiocytosis, chronic or chronic-active inflammation and bronchiolar-alveolar hyperplasia, all which followed dose-dependent trends with respect to severity (REACH; Oller et al., 2008).

The LOAEC based on respiratory effects was reported as 0.1 mg/m^3. However, Oller et al. highlight the concern that the equivalent deposited dose in the pulmonary region of humans is likely to be different and therefore the LOAEC should be re-assessed for risk assessment purposes in humans (Oller et al., 2008).

Genotoxicity

There are limited in vitro and in vivo genotoxicity data for this chemical. Based on the effects reported below, there is insufficient evidence to warrant a hazard classification.

Various non-guideline in vitro studies are described below:

In vitro studies:

- Nickel metal powder (unknown concentration) was reported to have a relative transformation potency 1.1 times that of nickel oxide in the BHK-21 cell line (REACH).
- A study conducted in Chinese hamster ovary (CHO) and Syrian hamster embryo (SHE) cells showed that incubation with 5, 10 or 20 μg/mL nickel showed weak transforming activity in CHO cells but not SHE cells (REACH).
- A study conducted in CHO cells showed that incubation with nickel metal (10 or 20 μM) resulted in abnormal cell cycle progression (S-phase accumulation) (REACH).
- A study in TK6 cells incubated with 800–1000 μM nickel metal induced slow-growth mutations, but did not induce any hypoxanthine-guanine phosphoribosyltransferase (HPRT) or normal growth mutations.
- A study conducted in primary human leucocytes and human cell strains WI.38 and MRC5 reported that exposure to nickel powder (unknown concentration) did not induce chromosome aberrations (REACH).

In vivo studies:

In an in vivo study conducted in rats (strain unspecified), rats were administered a single dose of nickel dust (2.5–5 mg/Ni, particle size <5μm) intratracheally and observed for 1–1.5 months. There was a 14-fold increase in chromosome aberrations in treated animals compared with controls. Similarly there was an increase in micronuclei and sister chromatid exchanges in treated animals compared with controls. However, the study is not well reported with no statistical information provided (REACH; EU RAR, 2008).

Carcinogenicity

The chemical is classified as hazardous—Category 3 carcinogenic substance—with the risk phrase ‘Limited evidence of carcinogenic effect’ (Xn; R40 in HSIS (Safe Work Australia). The International Agency for Research on Cancer (IARC) has classified nickel metal as ‘Possibly carcinogenic to humans’ (Group 2B) (IARC, 1990). Epidemiological evidence for carcinogenicity in humans exposed to metallic nickel alone has not been found, although epidemiological studies have shown an elevated risk of lung or nasal cancers in workers who were exposed to metallic nickel together with other nickel compounds.

Therefore, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend the current classification.

Animal data

The main carcinogenicity study carried out similarly to OECD TG 451 has been summarised in the **Repeated dose toxicity—inhalation** section of this report. Neoplastic evaluation showed a significant dose dependent increase in phaeochromocytomas (benign, malignant and combined) of the adrenal medulla in male rats (0.4 mg/m^3) compared with controls. The authors note that the control animals had a particularly low incidence of phaeochromocytomas compared with historical controls. In females (0.4 mg/m^3), there was a significant dose-dependent increase in the combined incidence of adenomas and carcinomas of the adrenal cortex, but not when analysed separately. The incidence of adrenal cortical adenomas was noted to be in the range of that noted for historical controls. Further carcinogenicity assessment of the complete respiratory tract did not show an increased incidence of respiratory tumours (REACH; Oller et al., 2008). An addendum to the 2008 European Union Risk Assessment Report (EU RAR) for nickel metal published by the Danish Environmental Protection Agency concluded that the two-year repeated dose inhalation study had limitations with respect to valid exposure duration for carcinogenicity assessment to be performed adequately. That is, not all animals were exposed to all dose levels until the end of the study due to termination of certain dose groups (females in the 0.4 mg/m^3 and males and females in the 1.0 mg/m^3) because of excessive mortality (EU RAR, 2009). However, the authors of the study consider the study to validly meet the exposure duration criterion in TG 451 by achieving acceptable duration of exposure (19–24 months) at two exposure levels, sufficiently high toxicity and sufficiently high surviving animals (Oller et al., 2008).

The finding with respect to adrenal tumours is questionable as these tumours are at a site remote from the inhalation exposure. In the oral carcinogenic study of nickel sulfate hexahydrate (NICNASa), no respiratory toxicity nor increased incidence of neoplasms of the adrenal glands were seen despite the blood nickel levels being several-fold higher than in the inhalation study on nickel metal. Therefore, it is possible that the observed phaeochromocytomas of the adrenal medulla could be secondary to lung toxicity, and not due to the direct effect of nickel ions on the adrenal glands (Oller et al., 2008).

Other studies on nickel metal, described as being conducted poorly, have been summarised in the EU RAR (2008) for nickel. In summary, exposure to nickel metal via inhalation or intratracheal administration is related to the development of local neoplasms of the respiratory tract. Further studies using other routes of administration (subcutaneous or intramuscular) have also yielded positive results with respect to local neoplasms or sarcomas respectively, although these routes of exposure are not considered relevant for human routes of exposure and the localised doses are not physiologically relevant (EU RAR, 2008).

Epidemiological data

The International Committee on Nickel Carcinogenesis in Man (ICNCM) study concluded that more than one form of nickel (soluble, oxidic, sulfidic and/or metallic) is associated with lung and nasal cancers in humans (Doll, 1990). For nickel metal alone, out of a cohort of 813 workers exposed to nickel metal powder, nine workers died from lung cancer. However, this was a lower rate compared with an average control death rate of 16.52 for lung cancer in the US. No nasal cancers were reported in this cohort of workers exposed to metallic nickel. The ICNCM study went on to further conclude that there was no evidence that metallic nickel was associated with increased lung and nasal cancer risks (Doll, 1990).

One case-control study conducted in a cohort of Norwegian nickel-refinery workers showed a clear dose-related effect for soluble nickel and lung cancer. The exposure to metallic nickel was reported to be correlated (r = 0.71) with soluble nickel compounds, indicating that exposure to nickel metal and soluble nickel compounds together was associated with the incidence of lung cancer (EU RAR, 2008).

In a study of hydrometallurgical refinery workers, analysis of 718 workers exposed to metallic nickel concentrations ranging from 0.2–49 mg/m^3 did not show an increased risk of cancer (Egedahl et al., 1993). A further update of this cohort was reported in 2001, and this assessed male employees who had worked in the refinery continuously for at least 12 months and were followed up for up to 17 years. As previously reported, no association was found between exposure to nickel concentrate or nickel metal and the development of respiratory cancers (Egedahl et al., 2001).

A review of two studies by the Agency of Toxic Substances and Disease Registry (ATSDR) concluded that 'there was no evidence that metallic nickel is associated with increased lung or nasal cancer risks in nickel workers' (ATSDR, 2005).

Reproductive and Developmental Toxicity

No data are available for this chemical.

Data available for previously assessed soluble nickel compounds (NICNASb) indicate that the Ni^{2+} ion is the determining factor for developmental toxicity. However, as the release and absorption of nickel from metallic nickel is substantially lower than soluble nickel compounds, the systemic bioavailability and, therefore, developmental toxicity of nickel compounds is expected to be low (EU RAR, 2008).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local long-term effects (carcinogenicity) and local acute effects (skin sensitisation). This chemical may also cause harmful effects (alveolar proteinosis, alveolar histiocytosis, chronic or chronic active inflammation, and bronchiolo-alveolar hyperplasia) following repeated exposure through inhalation.

The critical health effects for risk characterisation depend on the likely exposure for the limited cohort of workers exposed to particulate nickel metal; the main effects are those after repeated exposure. Carcinogenic risks are less probable for members of the public or workers exposed to massive nickel metal; the main risk is skin sensitisation.

Public Risk Characterisation

Public exposure resulting from the commercial and site-limited uses identified in Australia is unlikely. Hence, the risk to the public is not considered to be unreasonable.

This assessment has not assessed the dermatological risk to the public from the use of articles manufactured with nickel metal or alloys of nickel metal in consumer goods.

Occupational Risk Characterisation

During use of the chemical, dermal and inhalation exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer, quality control analysis, and cleaning and maintenance of equipment. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical local long-term and local acute health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemical are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

The data available support an amendment to the hazard classification in HSIS (refer to **Recommendation** section).

Based on available data on nickel from animal studies, there is a concern that the current occupational exposure standard (1 mg Ni/m^3—inhalable fraction) for 'Nickel, metal' in HSIS may not sufficiently protect worker health. A concentration of 0.1 mg/m^3 nickel metal powder was identified in the inhalation repeated dose toxicity studies as a level at which severe effects are observed. The Scientific Committee on Occupational Exposure Limits (SCOEL) in the EU has proposed an exposure standard (0.005 mg/m^3—respirable fraction) for 'poorly soluble nickel chemicals', which includes nickel oxide, nickel subsulfide and nickel metal (SCOEL, 2011). The differences between rats and humans with respect to particle deposition in the alveolar region should be considered and quantified in considering appropriate exposure controls (SCOEL, 2011).

NICNAS Recommendation

A Tier III assessment may be necessary to provide further information as to whether the current exposure controls are appropriate to offer adequate protection to workers.

A Tier III assessment may be necessary should sufficient Australian data become available to characterise the risk factors associated with non-occupational nickel dermatitis from contact with consumer articles.

All other risks are considered to have been sufficiently assessed at the Tier II level, subject to implementing any risk management recommendations, and provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by skin contact (Xi; R43)*	May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23)*	Causes damage to organs through prolonged or repeated exposure through inhalation - Cat. 1 (H372)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)*	Suspected of causing cancer - Cat. 2 (H351)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from dermal and inhalation exposure to nickel metal should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker’s health;

- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

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