Nickel carbonates: Human health tier II assessment

11 April 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Carbonic acid, nickel(2+) salt (1:1)	3333-67-3
Nickel, (carbonato(2-))tetrahydroxytri-	12607-70-4
Nickel, (carbonato(2-))tetrahydroxytri-, tetrahydrate	39430-27-8

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

Grouping Rationale

This group of chemicals contains nickel carbonate, nickel hydroxycarbonate and its hydrated salt; nickel hydroxycarbonate tetrahydrate (CAS No. 39430-27-8). The chemicals may be grouped together for risk assessment purposes as it is expected that the physico-chemical properties will not vary greatly, leading to the compounds in this group having the same toxicity profile and related end uses. Similarities of toxicological significance include their sparing solubility in sweat and lung fluids, and ready solubility in gastric fluids (Oller, 2013).

Import, Manufacture and Use

Australian

The total volume of nickel carbonate (CAS No. 3333-67-3) introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was between 10000 and 100000 tonnes.

The following Australian industrial uses were reported by the National Pollutant Inventory (NPI) for carbonic acid, nickel(2+) salt (1:1) (CAS No. 3333-67-3):

The chemical (CAS No. 3333-67-3) has reported site-limited use including:

- as a chemical intermediate;
- as a catalyst;
- in electric components; and

- in wastewater treatment.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Galleria Chemica and the Substances and Preparations in the Nordic countries (SPIN) database.

The chemicals in this group have reported commercial use including:

- as corrosion inhibitors; and
- in paints and coatings.

The chemicals in this group have reported site-limited use including:

- in plating and surface finishing;
- in the manufacturing of nickel oxide;
- in the manufacturing of nickel pigments;
- in the colouring of ceramics and glass;
- as chemical intermediates; and
- as catalysts.

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 μg/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 μg/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 Worker Health and Safety Controls

Hazard Classification

Nickel carbonate (CAS No. 3333-67-3) is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Xn; R22 (Acute toxicity);

Xi; R43 (Skin sensitisation); and

Carc. Cat. 3; R40 (Carcinogenicity).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

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

Health Hazard Information

Limited data are available for this group of chemicals. To fill data gaps, data will be read-across (OECD, 2007) from nickel subsulfide (NTP, 1996; Oller, 2013) and/or nickel sulfate (NICNASa). Read-across from nickel sulfate (NICNASa) will be conducted for oral exposure as nickel sulfate and nickel carbonate release the Ni^{2+} ion into artificial gastric solutions at similar rates (Oller, 2013). For inhalation or dermal exposure, read-across will be conducted from nickel subsulfide as both nickel subsulfide and nickel carbonate release the Ni^{2+} ion into artificial fluids of the lung and sweat at similar rates (Oller, 2013). Therefore, nickel sulfate and nickel subsulfide can be considered close analogues (depending on the route of exposure), and relevant data can be used according to read-across principles (OECD, 2007) to assess the risks of chemicals in this group.

Toxicokinetics

Nickel compounds can be absorbed via inhalation, ingestion and to a limited extent following dermal exposure. The absorption of nickel chemicals and the release of the nickel ion is dependent on the compounds' solubility in the specified physiological solutions (gastric or interstitial). 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).

Inhalation

The majority of nickel carbonate (0.05 mg) administered via intratracheal instillation in mice (unspecified species) was eliminated within 12 days (EU RAR, 2008).

Oral

A study conducted in rats (unspecified species) administered nickel carbonate (250, 500 or 1000 mg/kg bw/day) for two months, demonstrated significant nickel accumulation in tissues (bones, heart, kidney, blood, spleen, intestine, testes, skin and liver) at the highest dose. This was attributed to the solubility of the compound in the stomach (gastric fluid) and absorption through the intestine (EU RAR, 2008).

A similar absorption and accumulation profile was demonstrated in calves fed nickel carbonate (62.5, 250, or 1000 mg/kg bw/day) for eight weeks. Significant increases in tissue levels of nickel were observed in serum, kidneys, vitreous humour, lung, testes, bile, tongue, pancreas, ribs, spleen, brain, liver and heart at the highest dose. The authors concluded that the absorption and retention of dietary nickel was related to the rate of nickel intake (EU RAR, 2008).

Dermal

No data are available.

Acute Toxicity

Oral

Nickel carbonate (CAS No. 3333-67-3) is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). The available data support this classification and the classification of other chemicals in this group.

Nickel hydroxycarbonate (CAS No. 12122-15-5; a chemical closely related to the chemicals in the group, but not listed on the Australian Inventory of Chemical Substances (AICS)), had moderate acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in female Sprague Dawley (SD) rats was determined to be 2000 mg/kg bw according to OECD Test Guideline (TG) 425 (Henderson et al., 2012a). Mortality was observed in rats administered 990, 1250, 2500 and 3100 mg/kg bw nickel hydroxycarbonate (CAS No. 12122-15-5). Further adverse events included hypoactivity and reduced faecal volume for all dose groups except the two lowest doses (630 and 790 mg/kg bw). Discolouration of the intestines was observed in rats exposed to 990 and 1250 mg/kg bw nickel hydroxycarbonate (CAS No. 12122-15-5). On necropsy, rats administered the two highest doses (2500 and 3100 mg/kg bw) showed discolouration of the liver and the stomach was filled with a green mass (Henderson et al., 2012a).

Dermal

No data are available.

Inhalation

The chemicals in this group were of very high acute toxicity in animal tests following inhalation exposure. The median lethal concentration (LC50) was determined to be 0.24 and >2.09 mg/L in male and female SD rats, respectively. Based on the available information a classification for acute toxicity (inhalation) is warranted (refer to **Recommendation** section).

In a study conducted according to OECD TG 403, male and female (females tested only at 2.09 mg/L) SD rats were exposed to nickel carbonate (CAS No. 3333-67-3) (0.053, 0.261, 1.06 or 2.09 mg/L) once over four hours. All five males exposed to 0.261 mg/L showed abnormal respiration, tremors, reduced faecal volume and discoloured lungs and intestines on necropsy. All five male animals in the 0.261 mg/L exposure group died within 3–5 days after exposure. At the highest dose, 4/5 males and 1/5 female animals died after exposure. Surviving animals in the highest exposure group showed severe adverse effects including weight loss, abnormal respiration, facial staining, hypoactivity, a hunched posture and discoloured lungs and intestines on necropsy (REACH).

Corrosion / Irritation

Skin Irritation

Nickel carbonate (CAS No. 3333-67-3) is reported to slightly irritate skin in animal studies. The effects are not sufficient to warrant a hazard classification.

In a study conducted similarly to OECD TG 404, three female New Zealand White rabbits were exposed to 1 g of a 50 % w/w mixture of nickel hydroxycarbonate (CAS No. unspecified) for four hours under occlusive conditions. Mild erythema at the treatment site was evident within 30–60 minutes of patch removal. The degree of irritation was reported to decrease with time and completely resolved within 72 hours. No further signs of abnormal behaviour or toxicity were reported (REACH).

Eye Irritation

In an eye irritation study in rabbits, nickel carbonate was found to be irritating with conjunctivitis and marked to dense corneal opacity observed at 24 and 48 hours, which resolved within the seven-day observation period (REACH). The severity of effects only met the classification criteria under the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and not the Approved Criteria (HSIS).

In a study conducted according to OECD TG 405, three female New Zealand White rabbits were exposed to 0.06 g of nickel hydroxycarbonate (CAS No. 3333-67-3) in one eye. All three animals showed signs of iritis (average Draize score 1), corneal opacity (average Draize score 1) and conjunctival chemosis (average Draize score 2). Corneal opacity resolved after three days, and iritis and conjunctivitis resolved after four days. No further signs of abnormal behaviour or toxicity were reported (REACH).

Sensitisation

Skin Sensitisation

No data from animal or human studies are available for this group of chemicals.

Based on bioelution data, the release of the Ni^{2+} ion into artificial sweat is six times greater for nickel hydroxycarbonate (6.8 % of total sample) compared with nickel oxide (0.16 % of total sample) (REACHb). Therefore, considering that nickel oxide is classified for skin sensitisation, and data which indicate that the Ni^{2+} ion is a significant inducer of skin sensitisation (ATSDR, 2005; EU RAR, 2008; Oller, 2013), a classification for skin sensitisation is recommended (refer to **Recommendation section**) for this group of chemicals.

Repeated Dose Toxicity

Oral

Based on the limited data available, this group of chemicals is not expected to cause serious damage to health by prolonged exposure if swallowed. Furthermore, data from nickel sulfate (NICNASa), which is more bioavailable than nickel carbonate via the oral route, suggest that classification is not warranted.

In a study conducted in male dairy calves, 23 calves were fed a diet supplemented with 0, 62.5, 250 or 1000 ppm nickel carbonate (CAS No. unspecified) from 13 to 21 weeks of age. Three animals per group were euthanised after the eight-week dosing period for histopathological evaluation and other animals returned to a normal diet. Adverse effects reported included significant reduction in feed intake and, therefore, weight loss was reported in the high dose (1000 ppm) group. This reduction in weight reverted to normal once the animals were put onto a normal diet. Histopathological examination of animals after eight weeks of dosing did not show any pathological abnormalities specific to nickel exposure. Kidney abnormalities were noted in both the control and nickel dosed animals (EU RAR, 2008).

In another study conducted in monkeys (*Macaca sinicus*), animals were exposed to 250–1000 ppm nickel carbonate (CAS No. unspecified) incorporated in their diet for four months. The study reported no significant changes in body weight or haematological parameters. No further details are available (EU RAR, 2008).

Dermal

No data are available.

Inhalation

No data are available for this group of chemicals. However, bioaccessibility studies conducted in artificial biological fluids (interstitial lung fluid and alveolar fluid) indicate that nickel subsulfide and nickel carbonate release the Ni^{2+} ion into biological solutions of the lung at similar rates (Oller et al., 2009; Oller, 2013). Therefore, based on the data available below for nickel subsulfide, a hazard classification is recommended for the chemicals in this group (refer to **Recommendation** section).

The National Toxicology Program (NTP) has conducted 13-week and two-year repeated dose inhalation studies (similar to OECD TG 453) using nickel subsulfide in male and female Fischer 344 (F344) rats and $B6C3F_1$ mice. The results of these studies are summarised below.

13-week studies

In both studies conducted in rats and mice, 10 males and 10 females were exposed to 0, 0.15, 0.3, 0.6, 1.2 or 2.5 mg/m^3 of nickel subsulfide (equivalent to 0, 0.11, 0.22, 0.44, 0.88 or 1.83 mg/m^3 of nickel) via inhalation for six hours a day, five days a week, for 13 weeks.

Observed adverse effects in rats included laboured respiration in the highest dose group (2.5 mg/m^3). Also at the highest dose, male rats had a significantly lower body weight and body weight gain. Compared with controls, the relative lung weights were significantly increased in all exposure groups. Haematological markers (neutrophil and erythrocyte counts) were minimally increased in rats across all exposure groups. Adverse effects of the lung included a significant increase in the number of alveolar macrophages, interstitial infiltration and chronic inflammation of the lung in all groups exposed to $\geq$0.3 mg/m^3. Furthermore, lymphoid hyperplasia of the bronchial and mediastinal lymph nodes was observed in rats exposed to $\geq$0.3 mg/m^3 and atrophy of the nasal olfactory epithelium increased with increasing exposure concentration (NTP, 1996).

Similar adverse effects were reported in mice exposed to nickel subsulfide for 13 weeks. In contrast to the study with rats, body weight or body weight gain was not affected in mice. Similar to the study with rats, relative lung weights of female mice exposed to 1.2 or 2.5 mg/m^3 were significantly increased. Lung specific effects included a significant increase in alveolar macrophages at

an exposure concentration ≥0.3 mg/m^3. Other lung effects included chronic inflammation, fibrosis and bronchial lymph node hyperplasia at ≥ 1.2 mg/m^3. Similar to the rat study, the severity of atrophy of the nasal olfactory epithelium increased with increasing exposure concentration (NTP, 1996).

Two-year studies

In the two-year study conducted with F344 rats, 63 males and 63 females were exposed to 0, 0.15 or 1 mg/m^3 nickel subsulfide (equivalent to 0, 0.11 or 0.72 mg/m^3 nickel) for six hours a day, five days a week for two years. Exposure to nickel subsulfide did not affect survival when compared with controls. Observable adverse effects included rapid and shallow breathing following each exposure period. Lung-specific effects included a significant increase in lung weights compared with controls across all exposure groups when assessed at seven and 15 months. Non-neoplastic lung pathology included fibrosis, chronic active inflammation in the lung and bronchial lymph node hyperplasia, which was significantly increased in males and females at an exposure concentration ≥ 0.15 mg/m^3. There was also a significant increase in atrophy of the olfactory epithelium in males and females and chronic active inflammation in the nose of females at the highest exposure dose (NTP, 1996).

In the two-year study conducted with B6C3F$_1$ mice, 80 males and 80 females were exposed to 0, 0.6 or 1.2 mg/m^3 nickel subsulfide (equivalent to 0, 0.44, 0.88 mg/m^3 of nickel) under the same conditions. Exposure to nickel subsulfide did not affect survival when compared with the controls. Observable adverse affects included rapid and shallow breathing following each exposure period. Lung-specific effects included a significant increase in lung weights compared with controls across all exposure groups when assessed at seven and 15 months. Non-neoplastic lung pathology included fibrosis, chronic active inflammation in the lung and bronchial lymph node hyperplasia, which was significantly increased in males and females at an exposure concentration ≥ 0.6 mg/m^3. Similarly to the study conducted in F344 rats, there was a significant increase in atrophy of the olfactory epithelium in males and females and a significant increase in acute inflammation and degeneration of the olfactory epithelium in females across both exposure concentrations, respectively (NTP, 1996).

Based on the two-year studies in F344 rats, a lowest observed adverse effect concentration (LOAEC) of 0.11 mg/m^3 nickel for non-neoplastic lung toxicity was reported.

Genotoxicity

Based on the available in vitro and in vivo genotoxicity studies, the chemicals in this group may be genotoxic, and are recommended for hazard classification (refer to **Recommendation** section).

In vitro studies

In a study conducted according to OECD TG 476, mouse lymphoma (L5178Y) cells were treated with nickel hydroxycarbonate (CAS No. 12122-15-5) at a range of concentrations with (10–230 μg/mL and 40–220 μg/mL) and without (10–170 μg/mL and 1–40 μg/mL) metabolic activation and incubated for four or 24 hours, respectively. Nickel hydroxycarbonate did not increase the frequency of mutations or induce clastogenic effects with or without metabolic activation (REACH).

In a study conducted similarly to OECD TG 476, a modified Chinese hamster ovary (CHO) cell line (AS52) was incubated with nickel carbonate (2.5–11.2 μg/mL of nickel) (CAS No. unspecified) for 24 hours. Assessment of cytotoxicity was conducted 6–8 days after exposure and reported as an LC50 of 14.9 μg/mL (5.8 μg/ml of nickel). With respect to genotoxicity, a non-significant increase in mutation frequencies was reported (REACH).

A further study conducted in CHO cells demonstrated that nickel carbonate (10–1000 μM) (CAS No. unspecified) with and without nitrilotriacetic acid (NTA) significantly increased the frequency of sister chromatid exchanges (SCEs) in a dose-dependent manner (REACH). In a similar study conducted in CHO cells, a single exposure of 0.4 μM nickel carbonate (CAS No. unspecified) with or without the presence of NTA significantly increased the frequency of SCEs (REACH).

In vivo studies

In a study conducted in SD rats, animals were exposed to nickel carbonate (CAS No. 3333-67-3) (10, 15, or 20 mg/kg bw) via intraperitoneal (i.p.) injection. Compared with control animals, a significant increase in DNA single strand breaks and DNA protein crosslinks was observed in the 15 and 20 mg/kg bw exposure groups (REACH). In a similar study using i.p. injection, SD rats were injected with nickel carbonate (CAS No. 3333-67-3) at 0, 5 10, 15, 20 or 40 mg/kg bw. Kidney, liver, lung and thymus gland nuclei were assessed for the presence of DNA single strand breaks and crosslinks three and 20 hours after administration. DNA interstrand crosslinks were detectable in kidney nuclei and single strand breaks were detected in lung and kidney nuclei. A dose-response relationship to single strand breaks and crosslinks was reported in kidney nuclei. No DNA damage was reported in nuclei of the thymus (REACH).

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)). No data are available for chemicals in this group. However, bioaccessibility studies have demonstrated that the release of Ni^{2+} from chemicals in this group is similar to that of nickel subsulfide in biological solutions of the lung (Oller et al., 2009; Oller, 2013). Therefore, using read-across data from nickel subsulfide, there is evidence to indicate that the chemicals in this group are carcinogenic, and are recommended for re-classification.

Nickel carbonate

In a study to assess the carcinogenicity of nickel carbonate (CAS No. 3333-67-3), female Wistar rats were given an intraperitoneal injection of nickel carbonate (1 mg) twice weekly for 25 weeks. The animals were then observed for 94 weeks after the dosing period. Compared with controls, there was no significant effect of nickel carbonate on survival or tumour incidence. However, the report indicates that the incidence of tumours was significantly higher compared with historical controls (REACH).

Nickel subsulfide

Nickel subsulfide is classified as hazardous—Category 1 carcinogenic substance—with the risk phrase 'May cause cancer by inhalation' (T; R49) in HSIS (Safe Work Australia).

Animal data

In a two-year study conducted with F344 rats, 63 males and 63 females were exposed to 0, 0.15 or 1 mg/m^3 nickel subsulfide (equivalent to 0, 0.11 or 0.72 mg/m^3 nickel) for six hours a day, five days a week for two years. There was a significant increase in the number of alveolar/bronchiolar adenomas or carcinomas in male and female F344 rats (1 mg/m^3 nickel subsulfide) after two years of exposure. Furthermore, there was a significant increase in the number of bilateral neoplastic lesions of the adrenal medulla in male ($\geq$0.15 mg/m^3) and female rats ($\geq$1 mg/m^3) exposed to nickel subsulfide. However, compared with the two-year study in rats, the study in $B6C3F_1$ mice exposed to 0, 0.6 or 1.2 mg/m^3 nickel subsulfide (equivalent to 0, 0.44, 0.88 mg/m^3 of nickel) for two years did not report a significant increase in the number of alveolar/bronchiolar adenomas or carcinomas in males or females after two years of exposure (NTP, 1996).

Epidemiological data

There are limited data with respect to epidemiological studies on the chemicals in this group. The International Agency for Research on Cancer (IARC) has highlighted studies with an increased risk of lung cancer from exposure to nickel subsulfide, although these were often mixed exposures, either with soluble nickel or oxidic nickel compounds. A cohort of nickel plant (Clydach—United Kingdom) cleaners exposed to insoluble nickel compounds (oxidic and sulfidic mainly) were reported to have a high rate of lung cancer. This study was taken as sufficient evidence of carcinogenicity in humans of nickel subsulfide (IARC, 2012).

Reproductive and Developmental Toxicity

No data are available for the chemicals in this group. However, bioaccessibility studies have demonstrated that the release of the Ni^{2+} ion from chemicals in this group is similar to that of soluble nickel compounds (nickel chloride and nickel sulfate) in artificial gastric fluid (Henderson et al., 2012b; Oller et al., 2013). Read-across data from nickel chloride and nickel sulfate indicate that the chemicals administered orally to experimental animals can result in postimplantation/perinatal mortality, and these chemicals are classified for developmental toxicity (NICNASa; NICNASb). Therefore, based on the similarity of oral availability of the chemicals of the group with the surrogates and on the principles of read-across (OECD, 2007), the chemicals in this group warrant classification for developmental toxicity (refer to **Recommendation** section).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (genotoxicity and developmental toxicity), local long-term effects (carcinogenicity), systemic acute effects (acute toxicity by the oral and inhalation routes of exposure) and local effects (skin sensitisation). The chemical may also cause eye irritation and harmful effects following repeated exposure through inhalation.

Public Risk Characterisation

The chemicals in this group have site-limited uses in Australia. Overseas, the chemicals have commercial and site-limited uses. Although the public may come into contact with articles or coated surfaces containing the chemical, it is expected that the chemical will be bound within the article or coated surface and hence will not be bioavailable. Therefore, the risk to the public is not considered to be unreasonable.

Occupational Risk Characterisation

During use of the chemicals, dermal, ocular and inhalation exposure of workers to the chemicals may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemicals at lower concentrations may also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term effects, local long-term effects and systemic local and acute health effects, these chemicals may pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemicals 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 data for nickel subsulfide, and considering the concentration of 0.11 mg/m^3 nickel identified in the inhalation repeated dose toxicity studies at which adverse effects are observed, there is a concern that the absence of exposure controls in the HSIS may not be protective of the health of workers. 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 determined and quantified in considering appropriate exposure controls (SCOEL, 2011).

NICNAS Recommendation

A Tier III assessment may be necessary to provide further information to determine the adequacy of protection to workers under the current exposure control framework.

All other risks are considered to have been sufficiently assessed at the Tier II level, subject to implementing any risk management recommendations, and the recommended amendment to the classification is adopted, and labelling 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 chemicals in this group are 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.

In the absence of specific data on chemicals in this group, data have been read-across from nickel subsulfide (NTP, 1996) and the NICNAS assessments of nickel chloride and nickel sulfate (NICNASa; NICNASb; OECD, 2007). Should empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for the specific chemical, this may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Very toxic by inhalation (T+; R26)	Harmful if swallowed - Cat. 4 (H302) Fatal if inhaled - Cat. 2 (H330)
Irritation / Corrosivity		Causes serious eye irritation - Cat. 2A (H319)
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)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)	Suspected of causing genetic defects - Cat. 2 (H341)
Carcinogenicity	Carc. Cat 1 - May cause cancer by inhalation (T; R49)	May cause cancer - Cat. 1A (H350i)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May cause harm to the unborn child (T; R61)	May damage the unborn child - Cat. 1B (H360D)

[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 oral, dermal and inhalation exposure to chemicals in this group 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;
- 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 *reparation 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

Agency for Toxic Substances & Disease Registry (ATSDR) Toxicological Profile for Nickel (2005). Accessed September 2013 at **http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=44**

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed October 2013 at **http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/ns2004criteriaforclassifyinghazardous**

European Union Risk Assessment Report (EU RAR) for Nickel Carbonate (2008). Accessed December 2013 at **http://esis.jrc.ec.europa.eu/**.

Galleria Chemica. Accessed December 2013. **http://jr.chemwatch.net/galleria/**

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at **http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html**

Henderson R G, Cappellini D, Seilkop S K, Bates H K& Oller AR, (2012b). Oral Bioaccessibility Testing and Read-Across Hazard Assessment of Nickel Compounds. Regulatory Toxicology and Pharmacology. Volume 63(1) pp. 20–28

Henderson R G, Durando J, Oller A R, Merkel D J, Marone P A& Bates H K (2012a). Acute oral toxicity of nickel compounds. Regulatory Toxicology and Pharmacology 62 (2012) pp. 425 - 432.

International Agency for Research on Cancer (IARC) 2012. IARC monographs on the evaluation of carcinogenic risks to humans. Nickel and Nickel Compounds. Volume 100c (A review of Human Carcinogens: Arsenic, metals, fibres and Dusts). Accessed September 2013 at **http://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C-10.pdf**

National Industrial Chemical Notification and Assessment Scheme (NICNASa). Tier II Human health assessment for Nickel sulfate. Australian Government Department of Health. Accessed December 2013 at **http://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments**

National Industrial Chemical Notification and Assessment Scheme (NICNASb). Tier II Human health assessment for nickel chloride. Australian Government Department of Health. Accessed December 2013 at **http://www.nicnas.gov.au/chemical-information/imap-assessments/imap-group-assessment-report?assessment_id=878**

National Pollutant Inventory (NPI). Accessed December 2013 at **http://www.npi.gov.au/index.html**

National Toxicology Program (NTP) 1996. Technical Report on toxicity studies of nickel subsulfide (CAS No. 12035-72-2) in F344/N Rats and B6C3F1 Mice (inhalation studies). U.S. Department of Health and Human Services. Accessed December 2013 at **http://ntp.niehs.nih.gov/**

Oller (2013). Read across approach for nickel compounds: Human health endpoints. Presentation by Adriana R. Oller (NiPERA). NICNAS meeting - February 14, 2013

Oller A R, Cappellini D, Henderson R G& Bates, H K (2009). Comparison of nickel release in solutions used for the identification of water-soluble nickel exposures and in synthetic lung fluids. Journal of Environmental Monitoring (11) pp 823 - 829.

REACH Dossier. [carbonato(2-)]tetrahydroxytrinickel (CAS # 12607-70-4). Accessed December 2013 at **http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances**

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Annex XVII (2009). Accessed September 2013 at **http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:164:0007:0031:EN:PDF**

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). AccessedDecember 2013 at **http://hsis.safeworkaustralia.gov.au/HazardousSubstance**

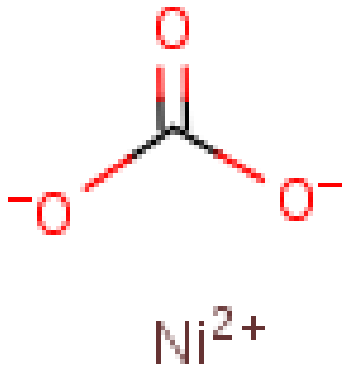
Scientific Committee on Occupational Exposure Limits (SCOEL). Recommendation on occupational exposure limits for nickel and nickel compounds (June, 2011). Accessed October 2013 at **http://ec.europa.eu/social/keyDocuments.jsp?advSearchKey=recommendation&mode=advancedSubmit&langId=en&policyArea=&type=0&country=0&year=2011**

Substances in Preparations in Nordic Countries (SPIN). Accessed December 2013 at **http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx**

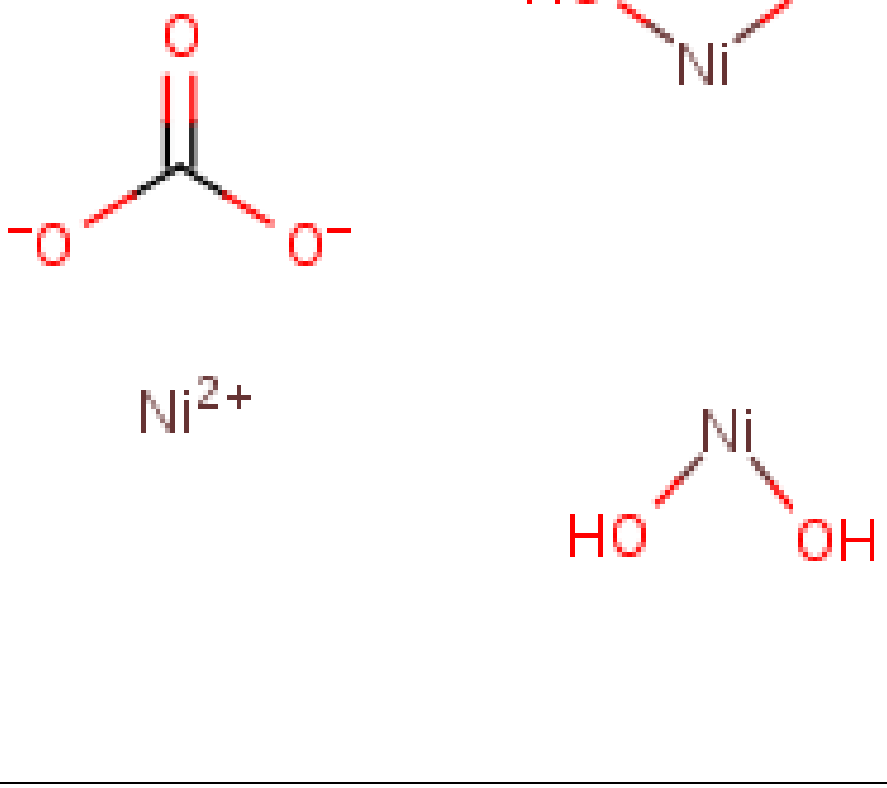
Work Health and Safety (WHS) Regulations 2011. Schedule 10 - Prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals. Accessed December 2013 at **http://www.comlaw.gov.au/Details/F2011L02664**

Last Update 11 April 2014

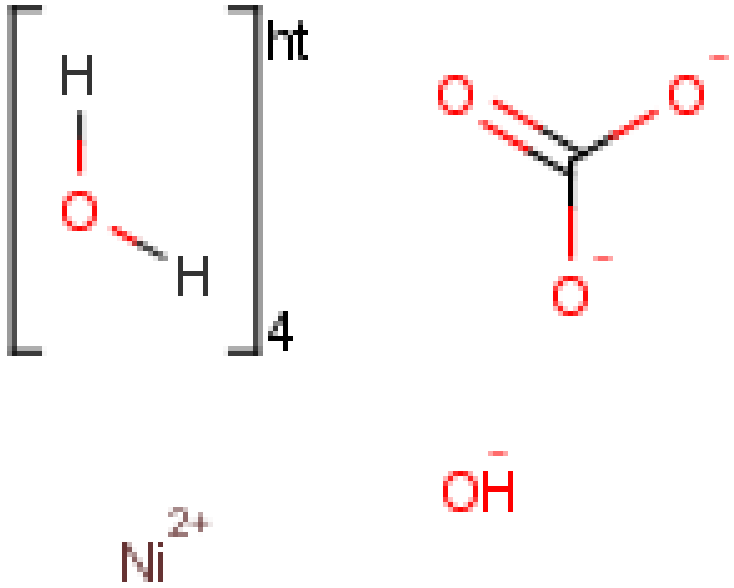
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Carbonic acid, nickel(2+) salt (1:1)** Nickel carbonate Nickel monocarbonate Nickelous carbonate
CAS Number	3333-67-3
Structural Formula	
Molecular Formula	CH2O3.Ni
Molecular Weight	118.7

Chemical Name in the Inventory and Synonyms	**Nickel, (carbonato(2-))tetrahydroxytri-** Nickel carbonate hydroxide Basic nickel carbonate Nickelous dihydroxynickel carbonate Nickel hydroxycarbonate
CAS Number	12607-70-4
Structural Formula	

	
Molecular Formula	CO3.HO.Ni
Molecular Weight	304.1

Chemical Name in the Inventory and Synonyms	**Nickel, (carbonato(2-))tetrahydroxytri-, tetrahydrate** Nickel carbonate hydroxide, tetrahydrate Nickel carbonate hydroxide hydrate Nickel hydroxycarbonate tetrahydrate
CAS Number	39430-27-8
Structural Formula	

	
Molecular Formula	CO3.4H2O.HO.Ni
Molecular Weight	207.8

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