Soluble nickel compounds (Group 1): Human health tier II assessment

07 February 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Acetic acid, nickel(2+) salt	373-02-4
Formic acid, nickel(2+) salt	3349-06-2
Sulfuric acid, ammonium nickel(2+) salt (2:2:1), hexahydrate	7785-20-8
Acetic acid, nickel(2+) salt, tetrahydrate	6018-89-9
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (2:3)	6018-92-4
Nickel bromide (NiBr2), trihydrate	7789-49-3
Nickel bromide (NiBr2)	13462-88-9
Sulfamic acid, nickel(2+) salt (2:1)	13770-89-3
Borate(1-), tetrafluoro-, nickel(2+) (2:1)	14708-14-6

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 consists of soluble nickel chemicals. The Ni (II) ion is considered to be the moiety responsible for systemic toxicity and a significant contributor to local toxicity (Henderson et al, 2012). Additional research (Henderson et al, 2012; Goodman et al, 2009) has highlighted the importance of bioaccessibility of nickel ions in different biological fluids (gastric fluid, interstitial fluid and sweat). This group of nickel chemicals has similar bioaccessibility and bioavailability; that is, these nickel chemicals release the Ni (II) ion into biological fluids at similar rates (Henderson et al, 2012; Goodman et al, 2009) and, therefore, can be assessed collectively.

Considering that nickel sulfate and nickel chloride have similar bioaccessibility and bioavailability in biological fluids to chemicals in this group, data available for nickel sulfate and nickel chloride can be "read across" when data are lacking for the chemicals in

this group.

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported by the National Pollutant Inventory (NPI).

Acetic acid, nickel (2+) salt (1:1) (CAS No. 373-02-4) has reported site-limited use as a:

- hydrogenation catalyst; and
- intermediate in the formation of other nickel compounds.

Sulfamic acid, nickel(2+) salt (2:1) (CSS No. 13770-89-3) has reported site-limited use in industrial plating.

No specific Australian use, import, or manufacturing information has been identified for other chemicals in this group.

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).

All chemicals in this group have the following common uses:

The chemicals have reported site-limited use including as:

- laboratory reagents;
- electroplating agents;
- chemical mediators (catalysts, accelerators, initiators); and
- chemical intermediates.

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 (WHS, 2011) for restricted use abrasive blasting at a concentration of greater than 0.1 % of nickel.

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 μg/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

The chemicals in this group are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

The group of chemicals falls under the category of 'Nickel, soluble compounds (as Ni)' in HSIS, and has an exposure standard of 0.1 mg/m^3 time weighted average (TWA) (HSIS).

International

The following exposure standards are identified for this group of chemicals (Galleria Chemica):

An exposure limit (TWA) of 0.05 - 1 mg/m^3 in different countries such as USA (in various states), Canada (in various provinces), Norway (0.05 mg/m^3), Greece (1 mg/m^3), Philippines (1 mg/m^3) and Switzerland (0.05 mg/m^3).

Health Hazard Information

Limited data are available for the acute oral toxicity of two compounds in this group (nickel acetate tetrahydrate and nickel sulfamate tetrahydrate) and skin irritation for nickel sulfamate tetrahydrate. Acute oral toxicity studies conducted in accordance

with OECD Test Guideline (TG) 425 reported median lethal doses (LD50s) as 550 and 1098 mg/kg bw for nickel acetate tetrahydrate and nickel sulfamate tetrahydrate respectively (Henderson et al, 2012; REACHa, REACHb). These data are consistent with LD50 values reported for other soluble nickel compounds which range from 300 – 1500 mg/kg bw (NICNASa; NICNASb; NICNASc). In the skin irritation study carried out according to OECD TG 404, nickel sulfamate tetrahydrate (CAS No not specified) was reported to cause erythema and oedema one hour after removal of the chemical, which resolved within the 14 day observation period (REACHb). As for acute oral toxicity, skin irritation data are consistent with those reported for other soluble nickel compounds (NICNASa; NICNASb; NICNASc). In the absence of further toxicological data for this group of chemicals, it is expected that the chemicals in this group will have a similar hazard profile to other soluble nickel compounds due to similar bioaccessibility and bioavailability in biological fluids (Oller et al, 1999; Henderson et al, 2012). Soluble nickel compounds assessed (nickel chloride and nickel sulfate) are currently classified for carcinogenicity, genotoxicity and developmental toxicity. In addition, soluble nickel compounds are classified for acute toxicity by the oral and inhalation routes of exposure, skin and respiratory sensitisation and skin irritation. Also, soluble nickel compounds are classified for repeat dose toxicity via inhalation. The available data for nickel sulfate and nickel chloride support an amendment to the classification for this group of chemicals (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), local and systemic acute effects (acute toxicity by the oral and inhalation routes of exposure) and local acute effects (skin and respiratory sensitisation). The chemical may also cause harmful effects on the respiratory tract following repeated exposure through inhalation and skin irritation.

Public Risk Characterisation

The majority of chemicals in this group have no identified uses in Australia except for nickel acetate (CAS No 373-02-4) and nickel sulfamate (CAS No 13770-89-3), which have site limited uses. Overseas, all chemicals in this group have site-limited uses. Therefore, it is unlikely that the public will be exposed to chemicals in this group. Although the public may come into contact with articles/coated surfaces containing the chemical, it is expected that the chemical will be bound within the article/coated surface and hence will not be bioavailable. Therefore the risk to the public is not considered to be unreasonable.

Occupational Risk Characterisation

Based on overseas use, it is possible that the chemicals of this group may be used for electroplating, as chemical mediators and chemical intermediates. During use of the chemicals in electroplating, dermal, ocular and inhalation exposure of workers to these 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, local long-term and systemic acute/local 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 available data on nickel sulfate hexahydrate from animal studies, there is a concern that the current occupational exposure standard (0.1 mg Ni/m^3 - inhalable fraction) for 'Nickel, soluble compounds (as Ni)' in HSIS may not be sufficiently protective of the health of workers. A concentration of 0.25 mg/m^3 nickel sulfate hexahydrate (CAS No. 10101-97-0) (equivalent

to 0.06 mg Ni/m^3) 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 proposed a lowering of the exposure standard to 0.01 mg Ni/m^3 (TWA - inhalable fraction) for water soluble and poorly water soluble nickel compounds, excluding metallic nickel (SCOEL, 2011). The differences between rats and humans with respect to particle deposition in the alveolar region should be considered and quantified in considering an exposure standard (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.

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

Public Health

It is recommended that the existing SUSMP classification for nickel sulfate be altered to "Nickel soluble salts" as it is likely that for any publicly available product containing nickel sulfate, other soluble nickel compounds including members of this group could be substituted.

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]
Acute Toxicity	Harmful if swallowed (Xn; R22) Harmful by inhalation (Xn; R20)	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Irritating to skin (Xi; R38)	Causes skin irritation - Cat. 2 (H315)
Sensitisation	May cause sensitisation by inhalation (Xn, R42) May cause sensitisation by skin contact (Xi; R43)	May cause allergy or asthma symptoms or breathing difficulties if inhaled - Cat. 1 (H334) 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)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
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 inhalation exposure to nickel chloride 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.

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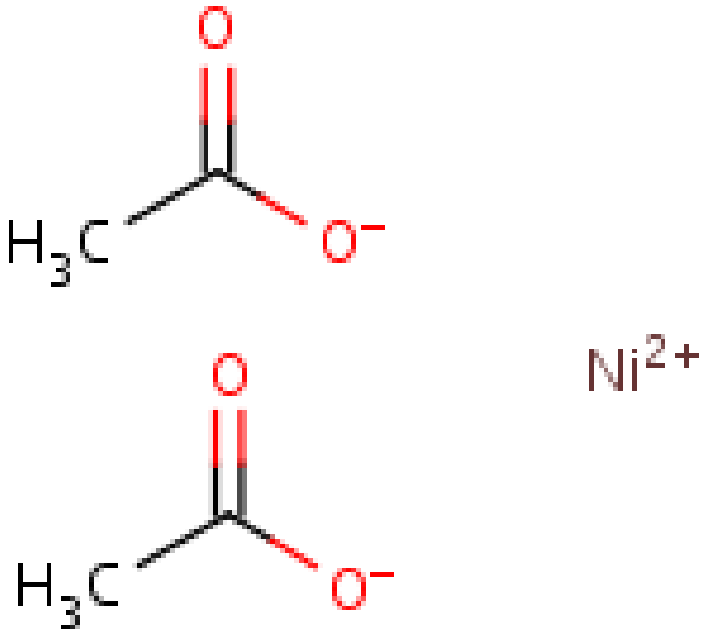
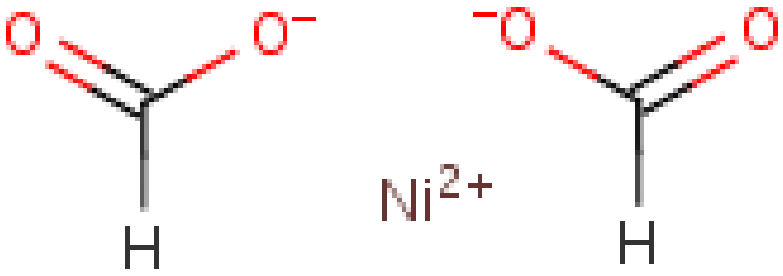
Chemical Identities

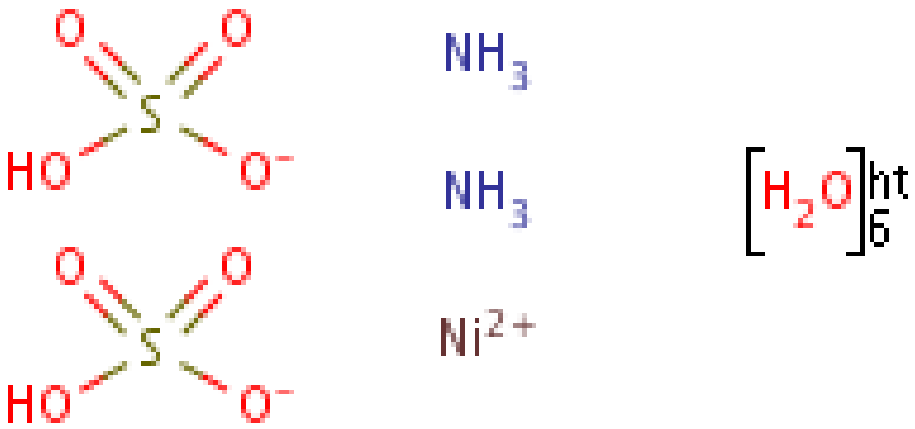
Chemical Name in the Inventory and Synonyms	**Acetic acid, nickel(2+) salt** Nickel acetate Nickel (II) acetate Nickel diacetate Nickelous acetate
CAS Number	373-02-4
Structural Formula	

	
Molecular Formula	C2H4O2.1/2Ni
Molecular Weight	176.8

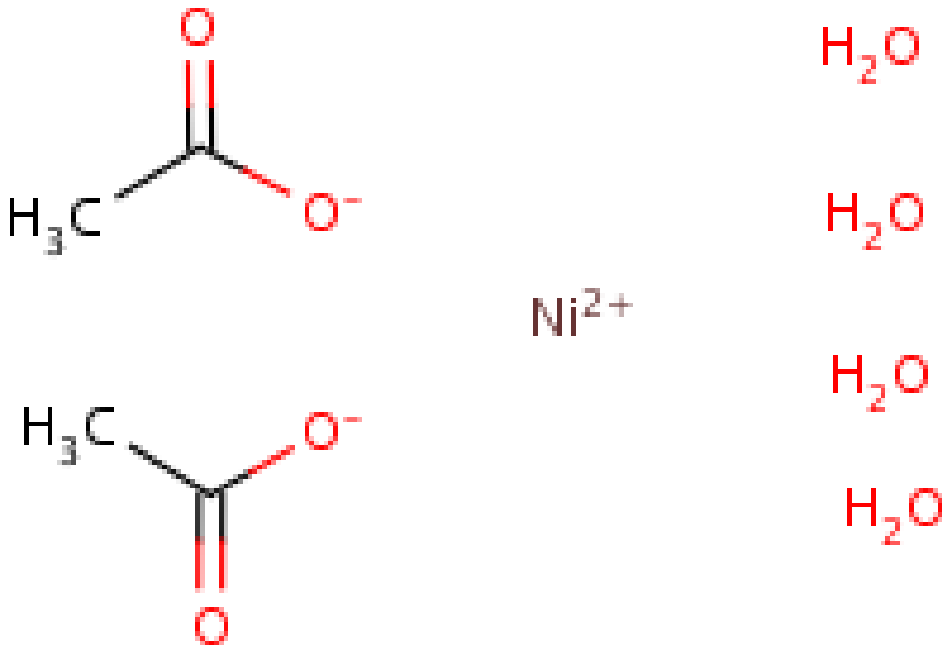
Chemical Name in the Inventory and Synonyms	**Formic acid, nickel(2+) salt** Nickel (II) formate Nickelous formate Nickel formate
CAS Number	3349-06-2
Structural Formula	

	
Molecular Formula	CH2O2.1/2Ni
Molecular Weight	184.76

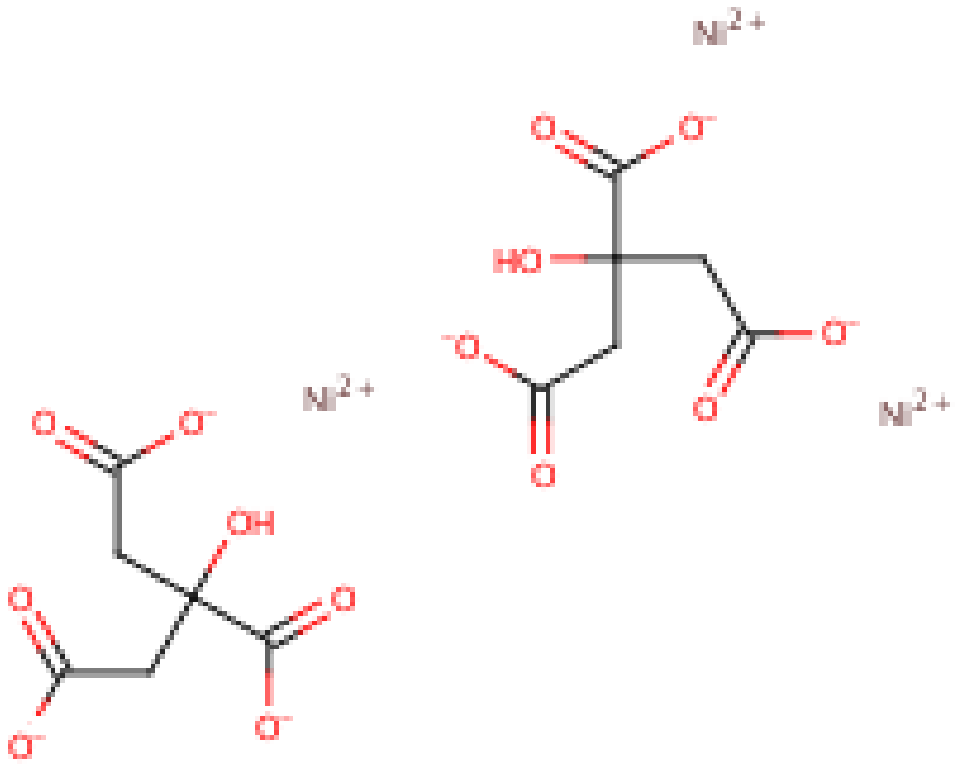
Chemical Name in the Inventory and Synonyms	**Sulfuric acid, ammonium nickel(2+) salt (2:2:1), hexahydrate** Nickel diammonium disulfate, hexahydrate Nickel ammonium sulfate hexahydrate Ammonium nickel(2+) sulfate hexahydrate
CAS Number	7785-20-8
Structural Formula	

	
Molecular Formula	H3N.H2O4S.3H2O.1/2Ni
Molecular Weight	394.99

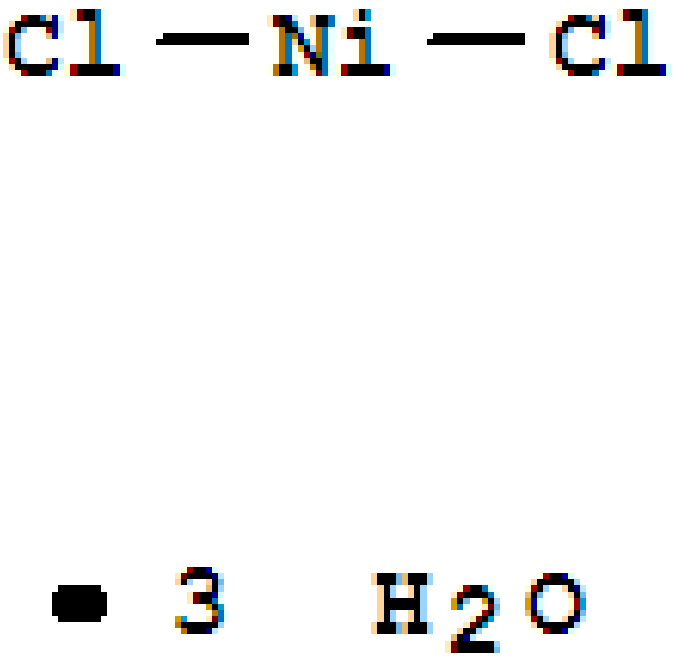
Chemical Name in the Inventory and Synonyms	**Acetic acid, nickel(2+) salt, tetrahydrate** Nickel diacetate, tetrahydrate Diacetatonickel tetrahydrate Nickelous acetate tetrahydrate Nickel (II) acetate tetrahydrate Nickel acetate [Ni(OAc)2.4H2O], tetrahydrate
CAS Number	6018-89-9
Structural Formula	

	
Molecular Formula	C2H4O2.2H2O.1/2Ni
Molecular Weight	248.84

Chemical Name in the Inventory and Synonyms	**1,2,3-Propanetricarboxylic acid, 2-hydroxy-, nickel(2+) salt (2:3)** Nickel citrate Triickel dicitrate Citric acid, nickel(2+) salt (2:3) (8CI)
CAS Number	6018-92-4
Structural Formula	

	
Molecular Formula	C6H8O7.3/2Ni
Molecular Weight	554.3

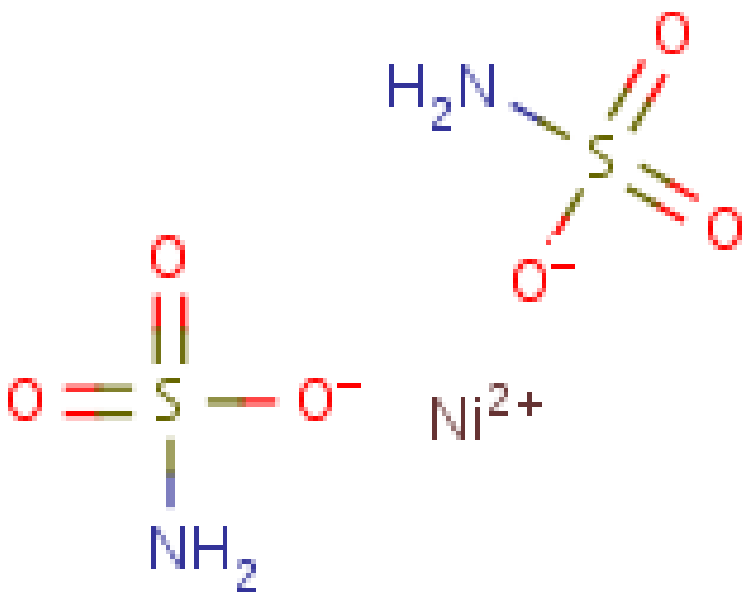
Chemical Name in the Inventory and Synonyms	**Nickel bromide (NiBr2), trihydrate** Nickel dibromide trihydrate
CAS Number	7789-49-3
Structural Formula	

	
Molecular Formula	Br2Ni.3H2O
Molecular Weight	272.55

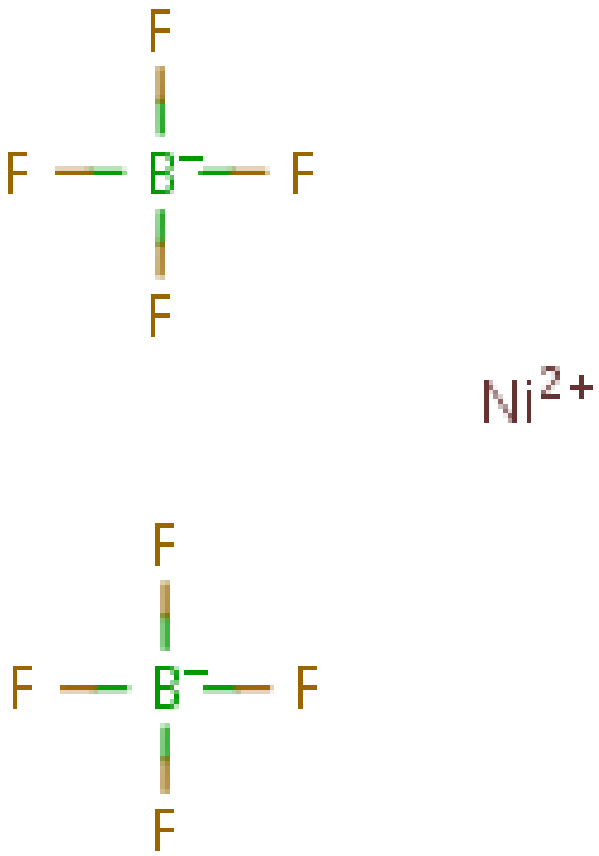
Chemical Name in the Inventory and Synonyms	**Nickel bromide (NiBr2)** Nickel dibromide Nickel (2+) bromide Nickelous bromide
CAS Number	13462-88-9
Structural Formula	

	
Molecular Formula	Br2Ni
Molecular Weight	218.53

Chemical Name in the Inventory and Synonyms	**Sulfamic acid, nickel(2+) salt (2:1)** Nickel sulfamate Nickel (II) sulfamate Nickel sulfamate (Ni(H2NSO3)2) Aeronikl 400 Aeronikl 575
CAS Number	13770-89-3
Structural Formula	

	
Molecular Formula	H3NO3S.1/2Ni
Molecular Weight	250.85

Chemical Name in the Inventory and Synonyms	**Borate(1-), tetrafluoro-, nickel(2+) (2:1)** Nickel borofluoride Nickel fluoroborate Nickel(II) tetrafluoroborate Nickelous tetrafluoroborate Nickel bis(tetrafluoroborate)
CAS Number	14708-14-6
Structural Formula	



Molecular Formula	BF4.1/2Ni
Molecular Weight	232.30

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