Nickel salts of 2-ethylhexanoic acid: Human health tier II assessment

07 February 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Hexanoic acid, 2-ethyl-, nickel(2+) salt	4454-16-4
Hexanoic acid, 2-ethyl-, nickel salt	7580-31-6

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 of chemicals consists of nickel salts of 2-ethylhexanoic acid (2-EHA). Compounds in this group, may also be referred to as nickel soaps or nickel salts of fatty acids, but the toxic effects of the 2-EHA anion are toxicologically distinct from other metal soaps. The compounds in this group are expected to have similar toxicity given that the health effects of exposure to these chemicals are driven by both the Ni^{2+} ion and the fatty acid component of these chemicals, 2-EHA. As nickel is normally only found in the +2 oxidation state, the two chemicals are expected to be substantially identical.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified for the 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 and the Substances and Preparations in the Nordic countries (SPIN) database.

Hexanoic acid, 2-ethyl-, nickel(2+) salt (CAS No. 4454-16-4) may have domestic and commercial use in paints and coatings.

Hexanoic acid, 2-ethyl-, nickel(2+) salt (CAS No. 4454-16-4) has reported site-limited use including:

- as a process regulator;
- as a catalyst; and
- in plastics.

No uses were identified for hexanoic acid, 2-ethyl-, nickel salt (CAS No. 7580-31-6).

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 in abrasive blasting at a concentration of greater than 0.1 % 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 $\mu g/cm^2$/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 Worker Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

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

The health hazards associated with the chemicals in this group are predominately driven by the Ni^{2+} ion. The fatty acid component of these chemicals, in this case 2-EHA, has been assessed by NICNAS. The chemical 2-EHA is classified for skin irritation and reproductive and developmental toxicity (refer to **Recommendation section**) (NICNASa). The skin irritation effects of 2-EHA are associated with the acidity of this chemical, and are not expected to be manifested by salts of 2-EHA.

The Ni^{2+} ion is considered to be the moiety responsible for systemic toxicity and a significant contributor to local toxicity (Henderson et al, 2012). Nickel salts of fatty acids are readily soluble in organic solvents (Landau, 2000) and are expected to release the Ni^{2+} in aqueous solutions. Considering that toxicological or bioaccessibility and bioavailability data are not available for the chemicals in this group, the health effects from exposure to the Ni^{2+} component of the metal fatty acid were read-across from studies on soluble nickel compounds. The assessed soluble nickel compounds (nickel chloride and nickel sulfate) are currently classified for carcinogenicity, genotoxicity, developmental toxicity, acute toxicity by the oral and inhalation routes of exposure, repeat dose toxicity via inhalation, skin and respiratory sensitisation and skin irritation (NICNASb; NICNASc).

The available data for soluble nickel compounds and 2-EHA support an amendment to the classification for this group of chemicals (refer to **recommendation section**) (NICNASa; NICNASb; NICNASc). Should bioaccessibility and/or bioavailability data become available, the extent to which the classification for soluble nickel compounds has been applied to this group of chemicals could be re-examined.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (genotoxicity, reproductive toxicity 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 chemicals may also cause harmful effects on the respiratory tract following repeated exposure through inhalation and skin irritation.

Public Risk Characterisation

The chemicals in this group have no identified uses in Australia. Overseas, it has been implied that metal soaps are used as driers in paints (Nora & Koenen, 2000; Landau, 2000), although no specific information has been identified to substantiate the use. Dermal exposure to low levels of the chemicals in formulated paints is considered to be of low likelihood and, therefore, the possible risk to the Australian 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 domestically and commercially in paints and coatings and in the manufacture of plastics. During use of the chemicals, 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 long-term systemic and local, and acute systemic and 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**).

There is also a concern that there is currently no exposure standard in the HSIS for these chemicals, as they do not fall into the category of soluble nickel compounds nor any of the specific HSIS listings.

NICNAS Recommendation

Should information become available that identifies use of these chemicals in Australia, a Tier III assessment may be necessary to provide further information as to whether exposure controls are required 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

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.

In the absence of specific data on chemicals in this group, data have been read-across from the NICNAS assessments of 2-EHA, nickel chloride and nickel sulfate (NICNASa, NICNASb; NICNASc; OECD, 2007). If 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) 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)
Carcinogenicity	Carc. Cat 1 - May cause cancer by inhalation (T; R49)	May cause cancer - Cat. 1A (H350i)
Reproductive and Developmental Toxicity	Repro. Cat 3 - Possible risk of impaired fertility (Xn; R62) Repro. Cat 2 - May cause harm to the unborn child (T; R61)	Suspected of damaging fertility - Cat. 2 (H361f) 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, ocular and inhalation exposure to the chemicals 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 *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

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at **http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf**

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Substances in Preparations in Nordic Countries (SPIN). Accessed November 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**

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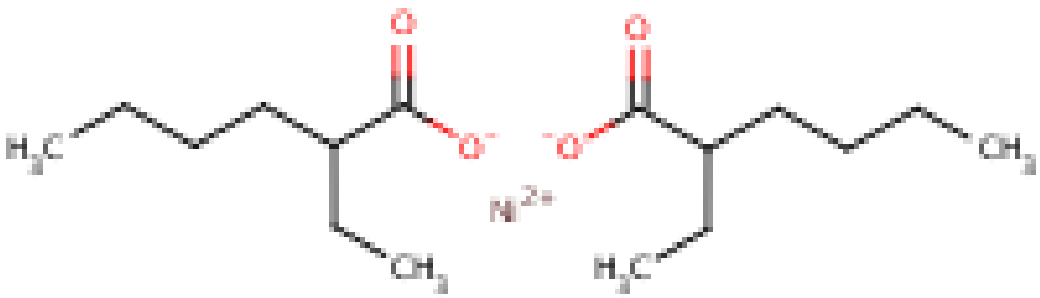
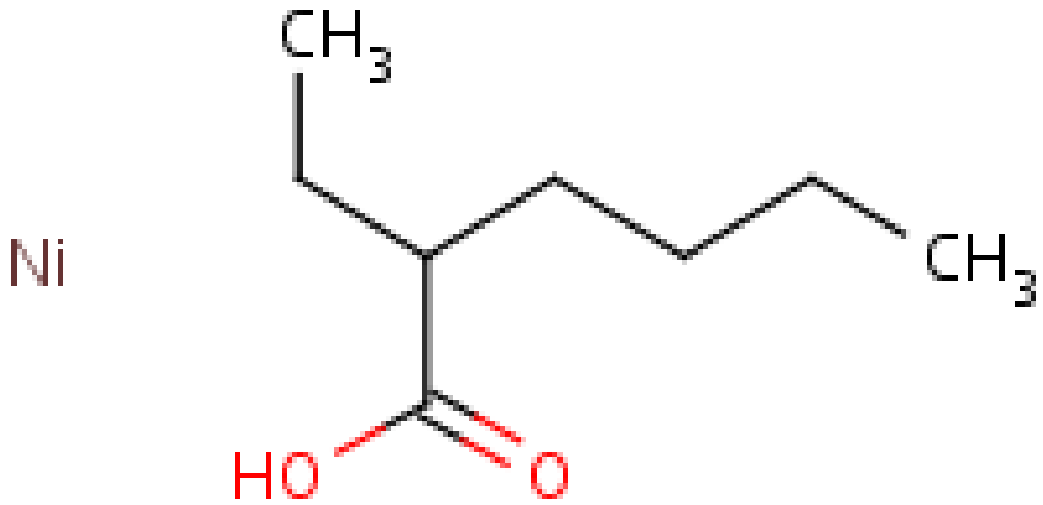
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Hexanoic acid, 2-ethyl-, nickel(2+) salt** Nickel bis(2-ethylhexanoate) Hexanoic acid, 2-ethyl-, nickel(2+) salt (2:1) Nickel 2-ethylhexanoate Nickel octoate Nickel 2-ethylhexoate
CAS Number	4454-16-4
Structural Formula	

Molecular Formula	C8H16O2.1/2Ni
Molecular Weight	345.10

Chemical Name in the Inventory and Synonyms	**Hexanoic acid, 2-ethyl-, nickel salt** Nickel 2-ethylhexanoate 2-Ethylhexanoic acid nickel (II) salt Nickel 2-ethylcapronate Nickel ethylhexanoate
CAS Number	7580-31-6
Structural Formula	
Molecular Formula	C8H16O2.xNi
Molecular Weight	202.91

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