Manganese slags: Human health tier II assessment

26 October 2018

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Slags, ferromanganese manufacturing	69012-28-8
Slags, silicomanganese manufacturing	69012-33-5

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

The inorganic chemicals in this group are substances of unknown or variable composition, complex reaction product, or biological material (UVCB). They are industrial by-products of the manufacture of ferromanganese or silicomanganese alloys, primarily containing oxides of manganese, aluminium, silicon, magnesium, calcium or barium. A 'high manganese content' is the only requirement in the production of these chemicals as a raw material for other uses (REACHa; REACHb).

It is expected that the three-dimensional structure of these chemicals will be aluminosilicate lattices, with the manganese (II) ions stabilised within the lattice. The chemicals are grouped together due to the expected similarity in their physico-chemical properties and related end uses.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers for the chemicals (REACHa; REACHb).

The chemicals have reported commercial uses as foundation materials (e.g. hard core) in construction.

The chemicals have reported site-limited uses as:

- additives in concrete, roads and surfaces manufacturing; and

- intermediates in the manufacture of manganese-containing alloys.

Restrictions

Australian

No known restrictions have been identified.

International

No known international restrictions have been identified for the specific chemicals in this group.

Manganese compounds are limited to 60 mg/kg (as Mn) as polymerisation aids for plastics intended to come into contact with food (Council of Europe Resolution AP (92) 2) (Galleria Chemica).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

The following exposure standard is identified for manganese compounds (Safe Work Australia) and considered relevant to the chemicals:

- manganese, dust and compounds (as Mn) have an exposure standard of 1 mg/m^3 time weighted average (TWA).

International

The following exposure standards are identified for manganese compounds (Galleria Chemica) and considered relevant to the chemicals:

- TWA values of 0.02–5 mg/m^3; and
- short-term exposure limit (STEL) values of 0.6–3 mg/m^3.

Health Hazard Information

The toxicity of the chemicals in this assessment is considered due to the presence of the manganese component. Some data are available for the chemicals. For end-points where data is lacking, health hazard information for manganese oxides (NICNASa) is considered a reasonable worst-case scenario. Although the chemicals are insoluble in water, bioaccessibility data for silicomanganese and ferromanganese slags confirm that these chemicals are bioaccessible, to a similar extent as the insoluble manganese oxides (see **Toxicokinetics** section).

Manganese oxides are classified for neurotoxicity following repeated oral and inhalation exposure, with manganese dioxide having additional classifications for acute oral and acute inhalation toxicity (NICNASa). The acute (see **Acute toxicity: Oral and Dermal** sections) and local effects (see **Irritation/Corrosivity** sections) of silicomanganese and ferromanganese slags are covered by data on the specific chemicals. However, data relevant to the long-term systemic effects of manganese compounds is based on epidemiological findings, not animal studies using specific manganese compounds. Therefore, human neurotoxicity data are considered relevant for these chemicals also, warranting hazard classification (see **Recommendation** section).

The report for manganese oxides (NICNASa) complements this assessment and should be read in conjunction with this assessment. The Tier II human health assessment for manganese oxides is available at: **https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-group-assessment-report?assessment_id=1627**.

Toxicokinetics

Availability of ionic species from silicomanganese slag was reported in a repeated dose toxicity study (according to the Organisation for Economic Cooperation and Development (OECD) Test Guideline (TG) 408). Sprague Dawley (SD) rats (n = 10/sex/dose) were exposed to silicomanganese slag by oral gavage at 0, 10, 100 or 1000 mg/kg bw/day for 90 days (see **Repeated dose toxicity: Oral** section). Blood samples were collected in weeks 7 and 13 of the study. There was no evidence of systemic toxicity. Based on results from the analysis of plasma collected at 7 weeks, it was concluded that manganese (as well as aluminium, barium and silicon) was not absorbed, since it was below the limit of detection (REACHa). No data were available for the samples collected at 13 weeks.

Ferromanganese slag is reported to have low water solubility (REACHb), and the same is expected for silicomanganese slag. Bioaccessibility is considered a better measure of in vivo bioavailability than water solubility. Dissolution of various manganese chemicals in artificial gastric and alveolar fluids was measured in a bioaccessibility study. For silicomanganese slag, relative manganese bioaccessibility (2 hours release) was measured to be <1 % in artificial gastric fluid and <0.01 % in artificial alveolar fluid. For ferromanganese slag, relative manganese bioaccessibility (2 hours release) was measured to be 24 % in artificial gastric fluid and <0.1 % in artificial alveolar fluid. By comparison, manganese (II) oxide (MnO; CAS No. 1344-43-0) and manganese oxide (Mn_3O_4; CAS No. 1317-35-7) had relative manganese bioaccessibilities (2 hours release) of approximately 12–13 % in artificial gastric fluid, and <0.01 % or 13 %, respectively, in artificial alveolar fluid. The relative manganese bioaccessibility (2 hours release) of manganese dioxide (MnO_2; CAS No. 1313-13-9) was <0.1 % in artificial gastric fluid and not detectable in artificial alveolar fluid (REACHa; REACHb). Based on other bioaccessibility studies, there is increased dissolution of metal compounds with longer exposure to the artificial fluids (Henderson et al., 2012).

Acute Toxicity

Oral

Based on the available data, the chemicals are considered to have low acute oral toxicity.

In an acute oral toxicity study (similar to EU Method B.1–Fixed Dose Procedure), SD rats (n = 5/sex) were exposed to silicomanganese slag at 2000 mg/kg bw once and observed for 14 days. There were no deaths and no signs of systemic toxicity (REACHa).

In an acute oral toxicity study (OECD TG 420), female Wistar rats (n = 5/dose) were exposed to ferromanganese slag at 300 or 2000 mg/kg bw once, and observed for 14 days. There were no deaths and no signs of systemic toxicity (REACHb).

Dermal

Based on the available data for silicomanganese slag, the chemicals are considered to have low acute dermal toxicity.

In an acute dermal toxicity study (similar to EU Method B.3–Fixed Dose Procedure), SD rats (n = 5/sex) were dermally exposed (semi-occlusive) to silicomanganese slag at 0 or 2000 mg/kg bw for 24 hours, before the chemical was removed by washing with water. Rats were observed for a total of 14 days. There was superficial skin damage at the site of contact that healed within the first week, but no deaths or signs of systemic toxicity (REACHa).

Corrosion / Irritation

Skin Irritation

Based on the available data, the chemicals are not considered to be irritating to skin.

In two separate in vivo skin irritation studies (OECD TG 404), male New Zealand White (NZW) rabbits (n = 3) were exposed (semi-occlusive) to 0.5 g silicomanganese slag or 0.5 g ferromanganese slag on shaved skin for 4 hours. The were no skin reactions during 72 hour observation periods and the primary dermal irritation index (PDII) was 0.0 for both studies (REACHa; REACHb).

In two separate in vitro skin irritation studies (similar to EU B.46), reconstructed human epidermis (EPISKIIN™) was exposed to 10 ± 2 mg silicomanganese slag or 10 ± 2 mg ferromanganese slag for 15 minutes, and observed for a 42 hour period. Tissue viability was then assessed and the relative mean viability was ≥ 100 % for all treated samples compared with controls. It was reported that the chemicals were not irritating (REACHa; REACHb).

In two separate in vitro skin corrosion studies (OECD TG 431), reconstructed human epidermis (SkinEthic™) was exposed to 20 mg silicomanganese slag or 20 mg ferromanganese slag for 3 or 60 minutes, and tissue viability assessed over a 3 hour period. The relative mean viability compared with controls was ≥91 % for all treated samples and it was reported that the chemicals were not corrosive (REACHa; REACHb).

Eye Irritation

Based on the available data, the chemicals are not considered to be irritating to eyes.

In two separate in vivo eye irritation studies (OECD TG 405), male NZW rabbits (n = 3) were exposed to 100 mg silicomanganese slag or 100 mg ferromanganese slag in the conjunctival sac of one eye, with the contralateral eye serving as control. Rabbits were observed for 72 hours post-treatment. In both studies, there were no corneal or iris effects, with average irritation scores of 0 over 24, 48 and 72 hours for each parameter. In all rabbits exposed to either chemical, there was conjunctival discharge at 1 hour, and conjunctival redness and chemosis were noted at 1 and 24 hours. These effects were fully reversed by 48 hours. The average conjunctival score over 24, 48 and 72 hours was 1.33/20 for silicomanganese slag and 4/20 for ferromanganese slag (REACHa; REACHb).

In two separate in vitro eye irritation studies, reconstituted corneal epithelium was exposed to 30 mg silicomanganese slag or 30 mg ferromanganese slag for 10 minutes, and cultures examined for viability after three hours. Relative mean viability was measured to be approximately 98 % in both studies for all treated samples compared with controls and it was reported that the chemicals were not irritating (REACHa; REACHb).

Sensitisation

Skin Sensitisation

Based on the available data for silicomanganese slag, the chemicals are not considered to cause sensitisation reactions.

In a local lymph node assay (OECD TG 429), female CBA/Ca mice (n = 4–5/dose) were topically exposed to 25 µL silicomanganese slag in dimethylformamide at 0, 2.5, 5 or 10 % w/w on the dorsal surface of each ear once daily for 3 days. Five days after the first treatment, mice were injected with radiolabelled methyl thymidine, before draining auricular lymph nodes

were excised and thymidine incorporation measured. The stimulation index (SI), or estimated concentration to produce a 3-fold increase in lymphocyte proliferation (EC3), was 0.85, 1.09 and 1.14 at 2.5, 5 and 10 % w/w concentrations, respectively. It was concluded that the chemical was not a skin sensitiser (REACHa).

Repeated Dose Toxicity

Oral

Only limited data are available for silicomanganese slags, showing grip strength changes at all dose levels and stomach effects in some animals at the mid- and high-dose levels. Overt manganese toxicity (including for manganese oxides (NICNASa), soluble manganese compounds (NICNASb) and elemental manganese (NICNASc)), is not generally evident in repeated dose toxicity studies in animals, except at high doses. However, based on oral bioaccessibility (see **Toxicokinetics** section) and the neurological effects reported in humans following chronic oral and inhalational manganese exposure (see **Other health effects: Neurotoxicity** section), the chemicals are recommended for classification as hazardous with hazard category 'Specific target organ toxicity (repeated exposure) – category 1' and hazard statement 'Causes damage to organs through prolonged or repeated exposure if swallowed or inhaled' (H372) (see **Recommendation** section).

In a repeated dose toxicity study (OECD TG 408), SD rats (n = 10/sex/dose) were exposed to silicomanganese slag at 0, 10, 100 or 1000 mg/kg bw/day for 90 days. There was one death in a male exposed at 100 mg/kg bw/day during week 8 of the study, but this was reported to be unrelated to treatment. Average body weight gains were similar in all groups, despite a 'consistently higher' food intake in rats exposed at 10 mg/kg bw/day compared with controls. Behavioural testing at 12 weeks revealed a statistically significant decrease in mean fore- and hind-limb grip strength in females exposed at the highest dose, and lower overall fore-limb grip strength in all treated male groups. Data for motor activity studies were not described in detail, but there were 'a few isolated statistical significances seen in the treated groups'. Data for sensory reactivity were not available. In haematological and clinical chemistry analyses in samples collected at 90 days, there were minor changes that were not considered treatment-related or toxicologically relevant. Organ weights were not significantly changed compared with controls. Macroscopic changes in the stomach (mucosal depression) were reported in 1 female at 100 mg/kg bw/day and 1 male at 1000 mg/kg bw/day. Histopathologically, effects in the stomach were observed in 1 female at 100 mg/kg bw/day and 4 males at 1000 mg/kg bw/day. In the non-glandular stomach, there was ulceration with inflammation and swelling, and in the glandular stomach there was hyperplasia with infiltration of inflammatory cells. Changes in the stomach were attributed to the hard granular nature of the chemical causing localised damage (REACHa).

Genotoxicity

Negative results were reported in a bacterial reverse mutation assay in *Salmonella typhimurium* strains TA 98 and 100 that were exposed to silicomanganese slags with and without metabolic activation. Cytotoxicity was not assessed (REACHa). No further details were available.

Based on the available data for manganese oxides (NICNASa) (as well as soluble manganese compounds (NICNASb)), the chemicals are not considered to be genotoxic.

Carcinogenicity

No data are available for the chemicals. Based on the available data for manganese oxides (NICNASa) (as well as soluble manganese compounds (NICNASb)), the chemicals are not considered to be carcinogenic.

Reproductive and Developmental Toxicity

No data are available for the chemicals for reproductive toxicity. Limited data are available for ferromanganese slags in a prenatal developmental toxicity study, showing some changes in implantation and resorption—however, these were not dose-dependent. Manganese oxides (NICNASa) (as well as soluble manganese compounds (NICNASb)) are not considered likely to have reproductive and developmental toxicity.

In a prenatal developmental toxicity study (OECD TG 414), female SD rats (n = 20/dose) were exposed to ferromanganese slag by oral gavage at 0, 100, 330 or 1000 mg/kg bw/day on gestation day (GD) 6–19, and euthanised on GD 20. In dams, there were no deaths or signs of systemic toxicity. Maternal terminal body weight (GD20) and overall body weight change (GD 6–20) were significantly reduced in all treated groups compared with control. Food intake was also lower in all treated groups compared with control. There were no abortions, but there was significantly increased post-implantation loss in the low- and mid-dose groups, as well as significantly increased early and total resorptions in the mid-dose group. These effects were not seen in the high-dose group. Placental weights were significantly increased in rats exposed at ≥330 mg/kg bw/day. Foetal body weights, litter size and live offspring numbers were not affected by treatment. External, skeletal and visceral malformations were not observed (NICNASb). The lowest observed adverse effect level (LOAEL) for maternal toxicity was 100 mg/kg bw/day based on changes in body weight, food intake and post-implantation loss at this dose level. Effects on foetal development were not seen at this level.

Other Health Effects

Neurotoxicity

Chronic inhalation and oral exposure to manganese impaired the central nervous system (CNS) function in humans (NICNASa; NICNASb), resulting in a syndrome known as manganism. Classification for neurotoxicity is; therefore, based on the disabling neurological effects observed in humans following chronic manganese exposure.

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is neurotoxicity.

Public Risk Characterisation

Given the uses identified for these chemicals, it is unlikely that the public will be exposed. Hence, the public risk from these chemicals is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, oral, dermal and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could 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 health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise exposure 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 the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other 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 are recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Repeat Dose Toxicity	Not Applicable	Causes damage to nervous system through prolonged or repeated exposure through inhalation and oral routes - Cat. 1 (H372)

[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 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 chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, 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 chemicals.

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 help meet 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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

References

Galleria Chemica. Accessed August 2018 at **http://jr.chemwatch.net/galleria/**

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Safe Work Australia (SWA). Hazardous Chemicals Information System (HCIS). Accessed August 2018 at **http://hcis.safeworkaustralia.gov.au/HazardousChemical**

Last Update 26 October 2018

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Slags, ferromanganese manufacturing** ferromanganese slag carbon ferromanganese
CAS Number	69012-28-8
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Slags, silicomanganese manufacturing** silicomanganese slag
CAS Number	69012-33-5
Structural Formula	No Structural Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

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