Iron chloride (FeCl3) and its hydrates: Human health tier II assessment

05 February 2016

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Iron chloride (FeCl3)	7705-08-0
Iron chloride (FeCl3), hexahydrate	10025-77-1

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

Entries for anhydrous chemicals on the Australian Inventory of Chemical Substances (AICS) are also taken to cover hydrates, although one hydrate of iron (iron(III) chloride hexahydrate (CAS No. 10025-77-1)) is independently listed on the inventory. The hydrates are toxicologically different from the anhydrous form of this chemical as the corrosive properties of the anhydrous chemical partly relate to its reaction with water. Aqueous formulations containing ferric chloride can be considered to contain the hydrates rather than the anhydrous chemical. As the CAS No. for the anhydrous form is considered to also apply to hydrates, these chemicals are grouped despite their toxicological differences.

When in aqueous solution, iron chloride and iron chloride hexahydrate are chemically and toxicologically indistinguishable. At high concentrations, the solutions, whether of anhydrous iron chloride or its hydrates, have very low pH due to hydrolysis to form hydrochloric acid.

Import, Manufacture and Use

Australian

Anhydrous iron chloride is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 10,000 and 99,999 tonnes.

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

The chemical has reported commercial use as an odour agent.

The chemical has reported site-limited uses including in:

- manufacturing of other chemicals; and
- engineering.

International

The following international uses of anhydrous iron chloride (CAS No. 7705-08-0) have been identified through:

- the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers;
- the Organisation for Economic Co-operation and Development Screening information data set International Assessment Report (OECD SIAR);
- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database;
- the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary;
- the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and
- various international assessments (OECD, 2004; OECD, 2007; CIUCUS, 2011).

The chemical has reported cosmetic uses, including as:

- an astringent; and
- a deodorant.

The chemical has reported domestic uses, including in:

- adhesives;
- paints, lacquers and varnishes; and
- surface treatments.

The chemical has reported commercial uses, including:

- in metal etching and engraving;
- in sewage and waste treatment;
- as a catalyst;
- as an electroplating agent;
- in disinfectants;
- as a flocculant;
- as a photographic agent;
- as a complexing agent;
- as a mordant; and
- as a chlorinating, condensing and oxidising agent.

The chemical has reported site-limited uses, including in manufacturing other chemicals.

The chemical has reported non-industrial uses, including as an:

- additive in animal feed; and
- astringent (pharmaceuticals).

Restrictions

Australian

Iron compounds including the two chemicals in this assessment are listed in schedules 2, 4, 5 and 6 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). The only restriction potentially relevant for industrial uses is a listing in schedule 5, relating to garden preparations. The schedule 6 entry relates only to animal treatment, while schedules 2 and 4 relate to human therapeutic use.

Schedule 5:

IRON COMPOUNDS:

a) for the treatment of animals (excluding up to 1 per cent of iron oxides when present as an excipient):

i) in preparations for injection containing 20 per cent or less of iron **except** in preparations containing 0.1 per cent or less of iron; or

ii) in other preparations containing 4 per cent or less of iron **except**:

A) in liquid or gel preparations containing 0.1 per cent or less of iron; or

B) in animal feeds or feed premixes; or

b) in garden preparations **except** in preparations containing 4 per cent or less of iron.

International

Iron chloride is listed on the Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist') (Galleria Chemica).

Existing Worker Health and Safety Controls

Hazard Classification

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

Exposure Standards

Australian

Soluble iron salts including iron chloride have exposure standards of 1 mg/m^3 time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit of 1 mg/m³ TWA and 2 mg/m^3 short-term exposure limit (STEL) occupational exposure limit (OEL) in different countries such as the United States (US), the United Kingdom, Canada and South Africa.

Health Hazard Information

Iron(III) chloride (CAS No. 7705-08-0), also called iron trichloride or ferric chloride, has the formula $FeCl_3$ with iron in the +3 oxidation state. The chemical will be referred to as iron chloride henceforth. Iron chloride hexahydrate is one of several isolatable hydrates of iron chloride.

Iron is an essential element in mammals. Approximately 70 % of iron in humans is stored in haemoglobin and about 5 - 10 % in myoglobin (OECD, 2004). When bound to normal haemoglobin and myoglobin, iron is in the ferrous (Fe^{2+}) form. Up to 25 % of iron in the body is in the ferric (Fe^{3+}) form and is stored as haemosiderin, ferritin, and transferrin in the liver, spleen, and bone marrow. Iron is an important component of a number of enzymes in mammals (Albretsen, 2006; OECD, 2007).

When iron chloride is dissolved in water, iron(III) cations and chloride anions are released. These ions, in low concentrations, are handled safely by the body under homeostatic control and as such the chemical is not expected to represent a risk of systemic toxicity at low concentrations.

Toxicokinetics

Anhydrous iron chloride was administered to rats by oral gavage in a toxicokinetic study. Iron was shown to be solubilised in the acidic gastric environment before chelating with proteins which retain the iron in soluble form, facilitating absorption in the small intestine (REACHa).

The principal site of iron absorption is the intestinal mucosa. Generally, 2-15 % of iron is absorbed from the gastrointestinal tract by the iron-binding glycoprotein transferrin.

Following absorption the majority of iron is bound to transferrin and transported to the bone marrow where it is incorporated into haemoglobin (OECD, 2007).

Excess ingested iron is typically excreted in bile, sweat, faeces and urine. Total iron excretion is usually of the order of 0.5 mg/day (OECD, 2004).

Acute Toxicity

Oral

Iron chloride has moderate acute toxicity based on an animal test following oral exposure. The median lethal dose (LD50) in mice is 1300 mg $FeCl_3$/kg bodyweight (bw). Iron chloride hexahydrate is expected to also have high acute toxicity with corrosive effects; however, no data are available.

The acute oral toxicity of iron chloride was assessed in female Queckenbusch mice (10 animals/dose group). The chemical was administered to mice by oral gavage in aqueous solution at 0, 186, 335, 604 or 1087 mg Fe/kg bw, (equivalent to 0, 540, 974, 1,756 and 3160 mg iron chloride/kg bw). Mortalities were 0/10, 1/10, 2/10, 8/10 and 10/10 for 540, 974, 1756 and 3160 mg/iron chloride/kg bw, respectively. On the basis of these results, an acute oral median lethal dose (LD50) of 1300 mg/kg bw was determined for iron chloride. No details were provided on clinical signs or histopathology (REACHa).

Dermal

No data are available for anhydrous iron chloride. However, a chemical which is similar to iron chloride hexahydrate (although not as corrosive), iron(III) sulfate (CAS No. 10028-22-5) has been assessed in the following study and is a suitable candidate for read-across. Based on this study, the chemical is expected to have low dermal acute toxicity except to the extent that toxicity is secondary to corrosivity.

In a dermal acute toxicity study conducted according to EPA Office of Pesticide Program TG 81-2 (acute dermal toxicity), iron(III) sulfate was applied to the skin of male and female rabbits (strain and group size not specified) at 2000 mg/kg bw. Few experimental details were provided; however, no mortalities occurred and as a result, a dermal LD50 of >2000 mg/kg bw was determined (REACHb).

Inhalation

Anhydrous iron chloride was assessed for inhalation toxicity in a non-guideline study in rats (strain not specified). Animals were exposed to a saturated atmosphere of aerosol generated from a 40 % aqueous solution of the test chemical. No mortalities were observed following exposure for eight hours. A median lethal concentration (LC50) could not be determined (REACHa).

Corrosion / Irritation

Corrosivity

Anhydrous iron chloride applied to intact rabbit skin produced corrosive effects following an exposure period of 20 hours. Considering there are no available skin irritation studies conducted according to guidelines with a four hour exposure period, a conservative approach indicates this chemical should be classified as corrosive. The hydrous form of iron chloride should also be considered corrosive based on results following application of aqueous solutions (see below).

Skin

Anhydrous iron chloride was assessed for skin irritation in a rabbit study (strain not specified). Few experimental details are available; however, the chemical (40 % (w/w) in water) was found to be irritating to the skin of rabbits after prolonged periods of exposure. The solution was applied to the back skin of animals for 1, 5, 15 minutes, or 20 hours. The solution was applied to the ear skin of another group of animals for 20 hours. Erythema was difficult to assess at longer time points given the solution stained the skin of animals. Signs of irritation were assessed one and eight days following exposure. Exposure to the back for 20 hours resulted in severe desquamation and scabbing when assessed eight days post-treatment. No signs of significant irritation were observed following shorter periods of exposure at any time point, at either test location (REACHa). The test substance was corrosive following an exposure period of 20 hours.

The same experimental conditions were adhered to in a parallel study which assessed the potential for anhydrous iron chloride to cause irritation. The chemical was applied to the back skin of rabbits (strain not specified) for one, five, 15 minutes or 20 hours. The chemical was also applied to the ear skin of another group of animals for 20 hours. The chemical was found to be corrosive to the skin of animals following a 20 hour exposure period. Exposure to the back skin for 20 hours resulted in slight necrosis, desquamation and scabbing (REACHa). Under the conditions of this study the chemical was corrosive following an exposure period of 20 hours.

Eye

Irreversible damage to corneal tissue and corrosion of the conjunctivae and eyelids were observed when the chemical was applied to the eyes. These effects were not reversible after 21 days.

In an eye irritation study, 50 mg of anhydrous iron chloride was applied to the eyes of rabbits. Several important experimental details were not reported, including the strain and number of rabbits used as well as some key specifics of the test, including whether eyes were rinsed following treatment. The eyes of animals were assessed for signs of irritation at one hour, 24 hours or eight days post-exposure. At one hour, palpebral conjunctivae were stained yellow, slight oedema, strong corneal opacity and ocular discharge were observed. These effects were not fully reversible within eight days. At 24 hours, palpebral conjunctivae were stained yellow, mild oedema, strong corneal opacity, corneal ablation and ocular discharge were observed. At eight days, palpebral conjunctivae were stained partly yellow and severe reddening, severe oedema, very severe corneal opacity and

suppurative inflammation were observed. Effects were not fully reversible within the eight-day observation period. Under these test conditions, anhydrous ferric chloride was corrosive to the eyes of rabbits following prolonged periods of exposure (REACHa).

Iron chloride was assessed in an eye irritation study in three female rabbits according to the Organisation of Economic Co-operation and Development (OECD) test guideline (TG) 405 (acute eye irritation/corrosion). The chemical (100 mg) was applied into the conjunctival sac of one eye of each animal. At one hour, and at days one, two, three, seven, 14, and 21, eye response and irritation in the cornea, iris and conjunctiva were evaluated and clinical signs were observed. Iridial abnormalities and diffuse areas of corneal opacity were observed in all animals at all time-points. Severe redness, oedema and excretion were observed in the conjunctivae of all the animals. Haemosiderosis and lymphocyte infiltration in the submucosa of the conjunctiva were observed histopathologically in one animal. Granulomatous inflammation was found in the conjunctiva and purulent keratitis was observed in the corneal stroma. These effects were not reversible within the observation period. On the basis of these findings, iron chloride was determined to be corrosive to the eyes of rabbits (REACHb; OECD, 2004).

Sensitisation

Skin Sensitisation

No data are available for iron chloride; however, a similar chemical; iron(III) sulfate, which is considered a relevant analogue for this endpoint, has been shown to be non-sensitising to skin in limited studies (OECD, 2004; REACHa; REACHb).

Iron(III) sulfate (CAS No. 10028-22-5) has been assessed for skin sensitisation in a Buehler test in guinea pigs. Very few experimental details are provided, although the study was reported to have been conducted according to TG US EPA OPP 81-6. The chemical was reported not to be a skin sensitiser (REACHa).

Repeated Dose Toxicity

Oral

No data available. However, no systemic toxicity is expected following oral exposure to the chemical at low concentrations.

Dermal

No data available. However, no systemic toxicity is expected following dermal exposure to the chemical at low concentrations.

Inhalation

No data available. However, no systemic toxicity is expected following inhalation exposure to the chemical at low concentrations.

Genotoxicity

No data available. However, no systemic toxicity is expected following exposure to the chemical at low concentrations.

Carcinogenicity

No data available. However, no systemic toxicity is expected following exposure to the chemical at low concentrations.

Reproductive and Developmental Toxicity

No data available. No systemic toxicity is expected following exposure to the chemical at low concentrations.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral exposure) and local effects (corrosivity).

Public Risk Characterisation

Use of the chemical in cosmetic and/or domestic products in Australia has not been identified. In the United States, one domestic product was identified in the US Household Products Database (US HPD). The product is an etchant with 32-45 % iron chloride (aqueous) used for etching circuit boards. Given the nature of the product it is likely to be used by hobbyists for a specialised function and hence, the public in general are not exposed to this chemical. It is expected that appropriate workplace health and safety labelling will be sufficient to manage the risk from the chemical in this product. Therefore, the public risk from this chemical is not considered to be unreasonable. The chemical is currently sufficiently risk managed (refer **Restrictions-Australian**).

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure may 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 chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic acute and local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure are implemented. The chemical 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 HSIS (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

Assessment of the chemical 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

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2015).

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 and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)	Harmful if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Causes burns (C; R34)	Causes severe skin burns and eye damage - Cat. 1B (H314)

[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 consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular and oral exposure to the chemical 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 that could 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;
- 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 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 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

Albretsen, J., 2006. Toxicology Brief: The Toxicity of Iron, an Essential Element. Veterinary Medicine.

Bailey, JE (ed.) 2011, Compilation of Ingredients Used in Cosmetics in the United States (CIUCUS), 1st Edition, Personal Care Products Council, Washington, D.C.

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Registration, Evaluation, Authorisation and Restriction of Chemicals (REACHb) dossier for iron dichloride (CAS No. 7758-94-3), accessed October 2015 at **http://echa.europa.eu/information-on-chemicals/registered-substances**

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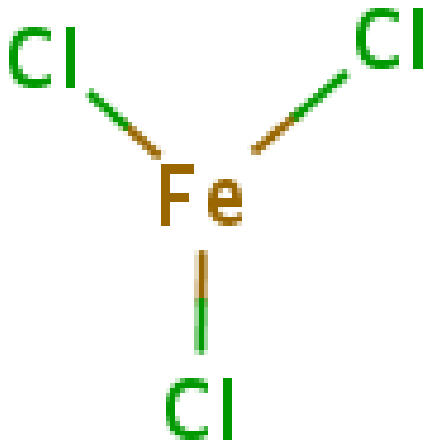
US National Library of Medicine's Hazardous Substances Data Bank (HSDB). Accessed October 2015 at **http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB**

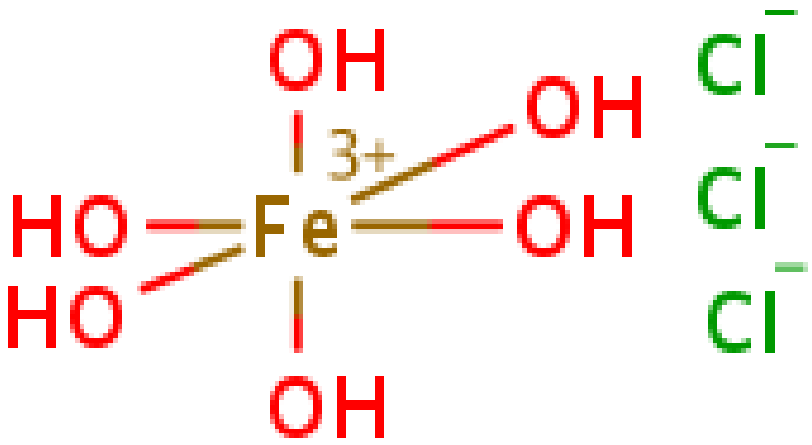
US National Library of Medicines, Household Products Database, Health& Safety Information on Household Products. Accessed October 2015 at **http://householdproducts.nlm.nih.gov/**

Last Update 05 February 2016

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Iron chloride (FeCl3)** ferric chloride iron trichloride anhydrous iron chloride
CAS Number	7705-08-0
Structural Formula	
Molecular Formula	Cl3Fe
Molecular Weight	162.20

Chemical Name in the Inventory and Synonyms	**Iron chloride (FeCl3), hexahydrate** Ferric chloride, hexahydrate Iron trichloride, hexahydrate Iron(III) chloride, hexahydrate
CAS Number	10025-77-1

Structural Formula	
Molecular Formula	Cl3Fe.6H2O
Molecular Weight	264.245

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