

# Hardock's Ironvita Blood & Oxygen International Animal Health Products Pty Ltd

Chemwatch: 4856-06

Version No: 9.1

Chemwatch Hazard Alert Code: 0

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# SECTION 1 Identification of the substance / mixture and of the company / undertaking

Safety Data Sheet according to Work Health and Safety Regulations (Hazardous Chemicals) 2023 and ADG requirements

### **Product Identifier**

Product name	Hardock's Ironvita Blood & Oxygen
Chemical Name	Not Applicable
Synonyms	Ironvita Blood & Oxygen
Chemical formula	Not Applicable
Other means of identification	Not Available

# Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses	Liquid iron and folic acid syrup for horses. Mix 30 - 45 mL in wet or dry feed or as directed by Veterinary Surgeon.
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# Details of the manufacturer or supplier of the safety data sheet

Registered company name	International Animal Health Products Pty Ltd	
Address	Healey Circuit Huntingwood NSW 2148 Australia	
Telephone	9672 7944	
Fax	61 2 9672 7988	
Website	www.iahp.com.au	
Email	info@iahp.com.au	

#### **Emergency telephone number**

Association / Organisation	Australian Poison Information Centre	
Emergency telephone numbers	13 11 26 (24 Hours)	
Other emergency telephone numbers	New Zealand: National Poisons Centre 0800 764 766 (24 hours)	

# **SECTION 2 Hazards identification**

### Classification of the substance or mixture

# NON-HAZARDOUS CHEMICAL. NON-DANGEROUS GOODS. According to the WHS Regulations and the ADG Code.

Poisons Schedule	Not Applicable	
Classification <sup>[1]</sup>	Hazardous to the Aquatic Environment Long-Term Hazard Category 2	
Legend:	1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI	

Hazard pictogram(s)	
Signal word	Not Applicable
Hazard statement(s)	
H411	Toxic to aquatic life with long lasting effects.
Not Applicable Precautionary statement(s)	
P273	Avoid release to the environment.
	Avoid release to the environment.
P273 Precautionary statement(s) P391 Precautionary statement(s)	Avoid release to the environment.  Response Collect spillage.
P273 Precautionary statement(s)	Avoid release to the environment.

# **SECTION 3 Composition / information on ingredients**

#### Substances

See section below for composition of Mixtures

#### **Mixtures**

CAS No	%[weight]	Name
1185-57-5	<5	ammonium ferric citrate
Not Available	balance	Ingredients determined not to be hazardous
Legend: 1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI; 4. Classification drawn from C&L * EU IOELVs available		

# **SECTION 4 First aid measures**

# Description of first aid measures

Eye Contact	<ul> <li>If this product comes in contact with eyes:</li> <li>Wash out immediately with water.</li> <li>If irritation continues, seek medical attention.</li> <li>Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.</li> </ul>
Skin Contact	<ul> <li>If skin or hair contact occurs:</li> <li>Flush skin and hair with running water (and soap if available).</li> <li>Seek medical attention in event of irritation.</li> </ul>
Inhalation	<ul> <li>If fumes, aerosols or combustion products are inhaled remove from contaminated area.</li> <li>Other measures are usually unnecessary.</li> </ul>
Ingestion	<ul> <li>Immediately give a glass of water.</li> <li>First aid is not generally required. If in doubt, contact a Poisons Information Centre or a doctor.</li> </ul>

# Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

For acute or short term repeated exposures to iron and its derivatives:

- Always treat symptoms rather than history.
- In general, however, toxic doses exceed 20 mg/kg of ingested material (as elemental iron) with lethal doses exceeding 180 mg/kg.
- Control of iron stores depend on variation in absorption rather than excretion. Absorption occurs through aspiration, ingestion and burned skin.
- Hepatic damage may progress to failure with hypoprothrombinaemia and hypoglycaemia. Hepatorenal syndrome may occur.

- Iron intoxication may also result in decreased cardiac output and increased cardiac pooling which subsequently produces hypotension.
- Serum iron should be analysed in symptomatic patients. Serum iron levels (2-4 hrs post-ingestion) greater that 100 ug/dL indicate poisoning with levels, in
  - excess of 350 ug/dL, being potentially serious. Emesis or lavage (for obtunded patients with no gag reflex) are the usual means of decontamination.
- Activated charcoal does not effectively bind iron.
- Catharsis (using sodium sulfate or magnesium sulfate) may only be used if the patient already has diarrhoea.
- Deferoxamine is a specific chelator of ferric (3+) iron and is currently the antidote of choice. It should be administered parenterally. [Ellenhorn and Barceloux: Medical Toxicology]

#### **SECTION 5 Firefighting measures**

#### Extinguishing media

- There is no restriction on the type of extinguisher which may be used.
- Use extinguishing media suitable for surrounding area.

#### Special hazards arising from the substrate or mixture

Fire Incompatibility	None known.

#### Advice for firefighters

Fire Fighting	<ul> <li>Alert Fire Brigade and tell them location and nature of hazard.</li> <li>Wear breathing apparatus plus protective gloves in the event of a fire.</li> <li>Prevent, by any means available, spillage from entering drains or water courses.</li> <li>Use fire fighting procedures suitable for surrounding area.</li> <li>DO NOT approach containers suspected to be hot.</li> <li>Cool fire exposed containers with water spray from a protected location.</li> <li>If safe to do so, remove containers from path of fire.</li> <li>Equipment should be thoroughly decontaminated after use.</li> </ul>
Fire/Explosion Hazard	<ul> <li>Non combustible.</li> <li>Not considered a significant fire risk, however containers may burn.</li> <li>May emit poisonous fumes.</li> </ul>
HAZCHEM	Not Applicable

#### **SECTION 6 Accidental release measures**

#### Personal precautions, protective equipment and emergency procedures

See section 8

# **Environmental precautions**

See section 12

#### Methods and material for containment and cleaning up

Minor Spills	<ul> <li>Clean up all spills immediately.</li> <li>Avoid breathing vapours and contact with skin and eyes.</li> <li>Control personal contact with the substance, by using protective equipment.</li> <li>Contain and absorb spill with sand, earth, inert material or vermiculite.</li> <li>Wipe up.</li> <li>Place in a suitable, labelled container for waste disposal.</li> </ul>
Major Spills	<ul> <li>Moderate hazard.</li> <li>Clear area of personnel and move upwind.</li> <li>Alert Fire Brigade and tell them location and nature of hazard.</li> <li>Wear breathing apparatus plus protective gloves.</li> <li>Prevent, by any means available, spillage from entering drains or water course.</li> <li>Stop leak if safe to do so.</li> <li>Contain spill with sand, earth or vermiculite.</li> <li>Collect recoverable product into labelled containers for recycling.</li> <li>Neutralise/decontaminate residue (see Section 13 for specific agent).</li> <li>Collect solid residues and seal in labelled drums for disposal.</li> <li>Wash area and prevent runoff into drains.</li> <li>After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.</li> <li>If contamination of drains or waterways occurs, advise emergency services.</li> </ul>

Personal Protective Equipment advice is contained in Section 8 of the SDS.

#### **SECTION 7 Handling and storage**

#### Precautions for safe handling

Safe handling

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.

	<ul> <li>Use in a well-ventilated area.</li> </ul>
	<ul> <li>Prevent concentration in hollows and sumps.</li> </ul>
	DO NOT enter confined spaces until atmosphere has been checked.
	<ul> <li>DO NOT allow material to contact humans, exposed food or food utensils.</li> </ul>
	Avoid contact with incompatible materials.
	When handling, DO NOT eat, drink or smoke.
	<ul> <li>Keep containers securely sealed when not in use.</li> </ul>
	<ul> <li>Avoid physical damage to containers.</li> </ul>
	Always wash hands with soap and water after handling.
	<ul> <li>Work clothes should be laundered separately. Launder contaminated clothing before re-use.</li> </ul>
	Use good occupational work practice.
	<ul> <li>Observe manufacturer's storage and handling recommendations contained within this SDS.</li> </ul>
	<ul> <li>Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.</li> </ul>
	Store in original containers.
	<ul> <li>Keep containers securely sealed.</li> </ul>
	Store in a cool, dry, well-ventilated area.
Other information	<ul> <li>Store away from incompatible materials and foodstuff containers.</li> </ul>
	Protect containers against physical damage and check regularly for leaks.
	Observe manufacturer's storage and handling recommendations contained within this SDS.

# Conditions for safe storage, including any incompatibilities

Suitable container	<ul> <li>1 L, 5 L and 25 L plastic containers.</li> <li>Check that containers are clearly labelled and free from leaks</li> <li>Packaging as recommended by manufacturer.</li> </ul>
Storage incompatibility	None known

# **SECTION 8 Exposure controls / personal protection**

# **Control parameters**

# Occupational Exposure Limits (OEL)

# INGREDIENT DATA

Source	Ingredient	Material name	TWA	STEL	Peak	Notes
Australia Exposure Standards	ammonium ferric citrate	Iron salts, soluble (as Fe)	1 mg/m3	Not Available	Not Available	Not Available

Emergency Limits				
Ingredient	TEEL-1	TEEL-2		TEEL-3
Hardock's Ironvita Blood & Oxygen	Not Available	Not Available		Not Available
Ingredient	Original IDLH		Revised IDLH	
ammonium ferric citrate	Not Available		Not Available	

# Exposure controls

Appropriate engineering controls	None required when handling small quantities. OTHERWISE:		
	Engineering controls are used to remove a hazard or place a barrier between the worker and the hazar engineering controls can be highly effective in protecting workers and will typically be independent of w provide this high level of protection.	•	
	The basic types of engineering controls are:		
	Process controls which involve changing the way a job activity or process is done to reduce the risk.		
	Enclosure and/or isolation of emission source which keeps a selected hazard "physically" away from the worker and ventilation that strategically "adds" and "removes" air in the work environment. Ventilation can remove or dilute an air contaminant if designed properly. The design of a ventilation system must match the particular process and chemical or contaminant in use.		
	Employers may need to use multiple types of controls to prevent employee overexposure.		
	Local exhaust ventilation usually required. If risk of overexposure exists, wear approved respirator. Corr obtain adequate protection. Supplied-air type respirator may be required in special circumstances. Corr ensure adequate protection.		
	An approved self contained breathing apparatus (SCBA) may be required in some situations.		
	Provide adequate ventilation in warehouse or closed storage area. Air contaminants generated in the w "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to e contaminant.		
	Type of Contaminant:	Air Speed:	
	solvent, vapours, degreasing etc., evaporating from tank (in still air).	0.25-0.5 m/s (50- 100 f/min.)	

	aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers, welding, spray drift, plating acid fumes, pickling (released at low velocity into zone of active generation)		
	direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion) grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).		1-2.5 m/s (200- 500 f/min.)
			2.5-10 m/s (500- 2000 f/min.)
	Within each range the appropriate value depends on:		
	Lower end of the range	Upper end of the range	
	1: Room air currents minimal or favourable to capture	1: Disturbing room air currents	
	2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity	
	3: Intermittent, low production.	3: High production, heavy use	
	4: Large hood or large air mass in motion	4: Small hood-local control only	
	generally decreases with the square of distance from the ext extraction point should be adjusted, accordingly, after referer extraction fan, for example, should be a minimum of 1-2 m/s meters distant from the extraction point. Other mechanical or apparatus, make it essential that theoretical air velocities are installed or used.	nce to distance from the contaminating source. (200-400 f/min) for extraction of solvents gener onsiderations, producing performance deficits w	The air velocity at th ated in a tank 2 rithin the extraction
Individual protection measures, such as personal protective equipment			
Eye and face protection	<ul> <li>No special equipment for minor exposure i.e. when handling small quantities.</li> <li>OTHERWISE:</li> <li>Safety glasses with side shields.</li> <li>Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lenses or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]</li> </ul>		
Skin protection	See Hand protection below		
Hands/feet protection	No special equipment needed when handling small quantities. OTHERWISE: Wear chemical protective gloves, e.g. PVC.		
Body protection	See Other protection below		
Other protection	No special equipment needed when handling small quantitie OTHERWISE: • Overalls.	S.	

# Recommended material(s)

#### GLOVE SELECTION INDEX

Glove selection is based on a modified presentation of the:

"Forsberg Clothing Performance Index".

The effect(s) of the following substance(s) are taken into account in the *computer-generated* selection:

Hardock's Ironvita Blood & Oxygen

Material	CPI
BUTYL	С
NATURAL RUBBER	С
NEOPRENE	С
PE/EVAL/PE	С
PVA	С
VITON	С

\* CPI - Chemwatch Performance Index

A: Best Selection

B: Satisfactory; may degrade after 4 hours continuous immersion

C: Poor to Dangerous Choice for other than short term immersion

**NOTE**: As a series of factors will influence the actual performance of the glove, a final selection must be based on detailed observation. -

#### Respiratory protection

Type A-P Filter of sufficient capacity. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

Where the concentration of gas/particulates in the breathing zone, approaches or exceeds the "Exposure Standard" (or ES), respiratory protection is required. Degree of protection varies with both face-piece and Class of filter; the nature of protection varies with Type of filter.

Required Minimum Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
up to 10 x ES	A-AUS P2	-	A-PAPR-AUS / Class 1 P2
up to 50 x ES	-	A-AUS / Class 1 P2	-
up to 100 x ES	-	A-2 P2	A-PAPR-2 P2 ^

#### ^ - Full-face

 $\begin{array}{l} \mathsf{A}(\mathsf{AII}\ \mathsf{classes}) = \mathsf{Organic}\ \mathsf{vapours},\ \mathsf{B}\ \mathsf{AUS}\ \mathsf{or}\ \mathsf{B1} = \mathsf{Acid}\ \mathsf{gasses},\ \mathsf{B2} = \mathsf{Acid}\ \mathsf{gas}\ \mathsf{or}\ \mathsf{hydrogen}\ \mathsf{cyanide}(\mathsf{HCN}),\ \mathsf{B3} = \mathsf{Acid}\ \mathsf{gas}\ \mathsf{or}\ \mathsf{hydrogen}\ \mathsf{cyanide}(\mathsf{HCN}),\ \mathsf{E} = \mathsf{Sulfur}\ \mathsf{dioxide}(\mathsf{SO2}),\ \mathsf{G} = \mathsf{Agricultural}\ \mathsf{chemicals},\ \mathsf{K} = \mathsf{Ammonia}(\mathsf{NH3}),\ \mathsf{Hg} = \mathsf{Mercury},\ \mathsf{NO} = \mathsf{Oxides}\ \mathsf{of}\ \mathsf{nitrogen},\ \mathsf{MB} = \mathsf{Methyl}\ \mathsf{bromide},\ \mathsf{AX} = \mathsf{Low}\ \mathsf{boiling}\ \mathsf{point}\ \mathsf{organic}\ \mathsf{compounds}(\mathsf{below}\ \mathsf{65}\ \mathsf{degC}) \\ \end{array}$ 

\* Where the glove is to be used on a short term, casual or infrequent basis, factors such as "feel" or convenience (e.g. disposability), may dictate a choice of gloves which might otherwise be unsuitable following long-term or frequent use. A qualified practitioner should be consulted.

# Ansell Glove Selection

The suggested gloves for use should be confirmed with the glove supplier.

# **SECTION 9** Physical and chemical properties

#### Information on basic physical and chemical properties

Appearance Brown liquid with a characteristic vanilla odour; mixes with water.

Physical state	Liquid	Relative density (Water = 1)	1.00-1.04
Odour	Not Available	Partition coefficient n- octanol / water	Not Available
Odour threshold	Not Available	Auto-ignition temperature (°C)	Not Applicable
pH (as supplied)	Not Available	Decomposition temperature (°C)	Not Available
Melting point / freezing point (°C)	Not Available	Viscosity (cSt)	Not Available
Initial boiling point and boiling range (°C)	Not Available	Molecular weight (g/mol)	Not Applicable
Flash point (°C)	Not Applicable	Taste	Not Available
Evaporation rate	Not Available	Explosive properties	Not Available
Flammability	Not Applicable	Oxidising properties	Not Available
Upper Explosive Limit (%)	Not Applicable	Surface Tension (dyn/cm or mN/m)	Not Available
Lower Explosive Limit (%)	Not Applicable	Volatile Component (%vol)	Not Available
Vapour pressure (kPa)	Not Available	Gas group	Not Available
Solubility in water	Miscible	pH as a solution (1%)	Not Available
Vapour density (Air = 1)	Not Available	VOC g/L	Not Available
Heat of Combustion (kJ/g)	Not Available	Ignition Distance (cm)	Not Available
Flame Height (cm)	Not Available	Flame Duration (s)	Not Available
Enclosed Space Ignition Time Equivalent (s/m3)	Not Available	Enclosed Space Ignition Deflagration Density (g/m3)	Not Available

# **SECTION 10 Stability and reactivity**

Reactivity	See section 7
Chemical stability	<ul> <li>Unstable in the presence of incompatible materials.</li> <li>Product is considered stable.</li> <li>Hazardous polymerisation will not occur.</li> </ul>
Possibility of hazardous reactions	See section 7

Conditions to avoid	See section 7
Incompatible materials	See section 7
Hazardous decomposition products	See section 5

# **SECTION 11 Toxicological information**

# Information on toxicological effects

Inhaled	The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified by EC Directives using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting. Not normally a hazard due to non-volatile nature of product	
Ingestion	The material has <b>NOT</b> been classified by EC Directiv of the lack of corroborating animal or human evidence	es or other classification systems as "harmful by ingestion". This is because e.
Skin Contact	The material is not thought to produce adverse health effects or skin irritation following contact (as classified by EC Directives using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting. Open cuts, abraded or irritated skin should not be exposed to this material	
Eye	Although the liquid is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may produce transient discomfort characterised by tearing or conjunctival redness (as with windburn).	
Chronic	Substance accumulation, in the human body, may occur and may cause some concern following repeated or long-term occupational exposure.	
Hardock's Ironvita Blood &	ΤΟΧΙΟΙΤΥ	IRRITATION
Oxygen	Not Available	Not Available
	τοχιςιτγ	IRRITATION
ammonium ferric citrate	dermal (rat) LD50: >2000 mg/kg <sup>[1]</sup>	Eye: no adverse effect observed (not irritating) <sup>[1]</sup>

# Oral (Mouse) LD50; 440 mg/kg<sup>[1]</sup> Skin: no adverse effect observed (not irritating)<sup>[1]</sup> Legend: 1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2. Value obtained from manufacturer's SDS. Unless otherwise specified data extracted from RTECS - Register of Toxic Effect of chemical Substances

AMMONIUM FERRIC CITRATE	Asthma-like symptoms may continue for months or even years after exposure to the material ends. This may be due to a non- allergic condition known as reactive airways dysfunction syndrome (RADS) which can occur after exposure to high levels of highly irritating compound. Main criteria for diagnosing RADS include the absence of previous airways disease in a non-atopic individual, with sudden onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. Other criteria for diagnosis of RADS include a reversible airflow pattern on lung function tests, moderate to severe bronchial hyperreactivity on methacholine challenge testing, and the lack of minimal lymphocytic inflammation, without eosinophilia. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. On the other hand, industrial bronchitis is a disorder that occurs as a result of exposure due to high concentrations of irritating substance (often particles) and is completely reversible after exposure ceases. The disorder is characterized by difficulty breathing, cough and mucus production. A high consumption of oxidised polyunsaturated fatty acids (PUFAs), which are found in most types of vegetable oil, may increase the likelihood that postmenopausal women will develop breast cancer. Similar effect was observed on prostate cancer, but the study was performed on mice Another "analysis suggested an inverse association between total polyunsaturated fatty acids and breast cancer risk, but individual polyunsaturated fatty acids behaved differently [from each other]. [] a 20:2 derivative of linoleic acid [] was inversely associated with the risk of breast cancer, PUFAs are prone to spontaneous oxidiation <i>Perovidation</i> . The feeding of lipid oxidation, products and oxidised fats has been reported to cause adverse biological effects on laboratory animals, including growth retardation, teratogenicity,

protein thiols (producing intermolecular cross-links) and, as a result produce functional impairment to enzyme systems, receptors and structural proteins. Aldehydes may also inhibit protein biosynthesis and increase osmotic fragility of lysosymes (releasing hydrolytic enzymes) and other subcellular organelles. They may also react with nucleic acids.

The toxicity of lipid hydroperoxides to animals is best illustrated by the lethal phenotype of glutathione peroxidase 4 (GPX4) knockout mice. These animals do not survive past embryonic day 8, indicating that the removal of lipid hydroperoxides is essential for mammalian life.

Peroxidised linoleic acid applied to the shaved skin of guinea pigs, in a patch test experiment, produced necrosis and bleeding. When the abdominal skin of guinea pig was patched for 8 days with a cream containing 25 nmol (in terms of malondialdehyde) of lipid peroxides per gram, a thickening of the epidermis was found

Lipid peroxidation in cellular membranes may produce several morphological alterations resulting, for example, in membrane aggregation, deformation or breakage. This may result in the release of hydrolytic enzymes which in turn may degrade functional macromolecules and cause secondary damage. In addition membrane-bound enzyme systems may be disrupted. No significant acute toxicological data identified in literature search.

Free radicals can readily react and damage cell membranes and genetic materials, sulphur containing amino acids, complex sugars and glycogen. It may induce allergic reaction and even cell death. Gene modification may result in tumour formation. ferroptosis, a non apoptotic form of cell death characterized by iron accumulation and uncontrolled lipid peroxidation, holds promise as a therapeutic approach in cancer treatment, alongside established modalities, such as chemotherapy, immunotherapy, and radiotherapy. However, research has raised concerns about its side effects, including damage to immune cells, hematopoietic stem cells, liver, and kidneys, the development of cachexia, and the risk of secondary tumor formation. ferroptosis leading to plasma membrane rupture and intracellular content release was Originally investigated as a targeted

therapy for cancer cells carrying oncogenic RAS mutations, ferroptosis . However, it can lead to side effects, including immune cell death, bone marrow impairment, liver and kidney damage, cachexia (severe weight loss and muscle wasting), and secondary tumorigenesis.

ecifically, the term 'ferroptosis, delineates a distinctive form of non-apoptotic cell demise marked by uncontrolled lipid peroxidation [. Traditional cell death effectors, such as caspases, GSDMD (gasdermin D), and MLKL (mixed lineage kinase domain like pseudokinase), are not essential for the process of ferroptosis [. Ferroptosis can be categorized as a type of regulated necrosis and exhibits some morphological characteristics reminiscent of necrotic cell features, such as plasma membrane rupture . Mechanistically, ferroptosis is mediated by the generation of toxic oxidized lipids, including 4-hydroxynonenal, as a result of lipid peroxidation . Additionally, advanced lipid peroxidation end products can lead to oxidative damage to proteins or nucleic acids, causing cellular dysfunction . Conversely, various antioxidant systems, comprising both GPX4 (glutathione peroxidase 4)-dependent and GPX4-independent pathways, play a context-dependent role in defending against ferroptosis

Erastin and RSL3 are two well-known small molecule compounds that are frequently used to trigger ferroptosis and explore the associated mechanisms of this cell death pathway.

Erastin is a novel compound capable of selectively killing engineered tumorigenic cells with RAS mutations, but not wild type cells. This cell death induced by erastin was found to be caspase-independent.

RSL3, is another compound that selectively kills RAS-mutant cells through a caspase-independent mechanism. In contrast to erastin, RSL3 activates a similar death mechanism, but in a mitochondrial VDAC (voltage-dependent anion channel)-independent manner.

sequent studies have shown that erastin-induced cell death in the fibrosarcoma cell line HT1080 and the lung cancer cell line Calu-1 relies on iron accumulation, consequent oxidative damage through the activation of the Fenton reaction, and inhibition of system xc- . System xc- is an amino acid antiporter that facilitates the exchange of extracellular cystine and intracellular glutamate across the cellular plasma membrane. It comprises a heavy chain component, SLC3A2 (solute carrier family 3 member 2), and a transport module, SLC7A11 (solute carrier family 7 member 11

Given the intricate connection between the ferroptotic process and oxidative stress-induced lipid peroxidation, the synergistic interplay of ROS amplification, lipid provisioning, and activation of lipid peroxidation enzymes collectively contribute to fostering ferroptosis induction or augmenting ferroptosis sensitivity

OS are chemically reactive molecules containing oxygen, typically produced as natural byproducts of cellular metabolism. They are essential for various physiological processes within cells. However, excessive accumulation of ROS can lead to oxidative stress, causing damage to cellular components (e.g., DNA, proteins, and lipids), and potentially contributing to various diseases. There are three main sources that generates ROS for ferroptosis

Mitochondria: Mitochondria serve as the primary source of ROS during oxidative phosphorylation, a process vital for cellular energy generation. Electrons escaping from the electron transport chain can react with molecular oxygen, leading to the production of O2-- (superoxide radicals), a type of ROS. Mitochondrial ROS can act as triggers for ferroptosis, while the presence of mitochondrial antioxidant systems, comprised of enzymatic and non-enzymatic antioxidants, can mitigate ferroptosis. Multiple mitochondrial metabolic pathways influence ATP (adenosine triphosphate) and ROS generation, thereby influencing ferroptosis sensitivity. For instance, glutaminolysis assumes particular importance in scenarios with limited glucose availability, such as in rapidly growing tumors. Cancer cells often depend on glutaminolysis to fulfill their high energy and biosynthetic demands. However, glutaminolysis can promote ferroptotic death triggered by deprivation of full amino acids or of cystine alone . The AMPK (AMP-activated protein kinase) functions as a critical cellular energy sensor. When activated in response to declining energy levels, AMPK promotes ATP production by enhancing the activity or expression of catabolic proteins. Simultaneously, it conserves ATP by inhibiting biosynthetic pathways. AMPK activation during energy deficiency can both inhibit ferroptosis, through phosphorylation of ACACA/ACC (acetyl-CoA carboxylase alpha) in MEFs (mouse embryonic fibroblasts) and human renal adenocarcinoma cells [68], and promote ferroptosis, by targeting BECN1 (beclin1)-mediated system xc- inhibition in human colorectal cancer cells or regulating pyrimidinosome assembly in human cervical cancer cells. These findings suggest the presence of a threshold for AMPK activity in regulating ferroptosis levels in cancer cells through various substrates or binding protein

NOXs (NADPH oxidases): These enzymes are specialized proteins that generate ROS as part of their normal function. While they serve crucial roles in immune responses and cellular signaling, they also contribute to ferroptosis. Increased expression of NOX can result in elevated ROS levels, thereby increasing sensitivity to ferroptosis . The activity of NOX in ferroptosis is subject to regulation by various factors. For example, the tumor suppressor protein TP53/p53 (tumor protein p53) can inhibit ferroptosis in human colorectal cancer cells by binding to DPP4 (dipeptidyl peptidase 4) [. Conversely, TP53 deficiency promotes the accumulation of DPP4 on the cell membrane, where it forms a complex with NOX1, resulting in oxidative damage . Arachidonic acid also has the capacity to enhance NOX1 activity through phosphorylation by PRKC/PKC (protein kinase C), thereby promoting ROS production . Furthermore, 4-hydroxynonenal, a byproduct of lipid peroxidation, augments NOX1 activity and induces ferroptosis in HT1080 and Calu1 cells. The ferroptosis-inducing effect of NOX1 activity can be counteracted by ALDH1B1 (aldehyde dehydrogenase 1 family member B1) in HT1080 and Calu-1 cells [6. ALDH1B1 catalyzes the oxidation of

aldehydes, converting them into their corresponding carboxylic acids, a process relevant to the development of colorectal and pancreatic tumors. The fenton reaction. The fenton reaction is a chemical process that occurs when H2O2 (hydrogen peroxide) interacts with a metal catalyst, usually Fe2+, resulting in the formation of highly reactive and destructive •OH (hydroxyl radicals) . This reaction is a notable contributor to oxidative stress and can cause damage to cellular components. Hydroxyl radicals target and harm the lipids found in cell membranes, namely lipid peroxidation. Lipid peroxidation can result in membrane destabilization, compromising the integrity of cells and potentially leading to ferroptosis. Apart from its involvement in the fenton reaction, iron can also enhance the activity of enzymes, such as ALOX (arachidonate lipoxygenase) family and POR (cytochrome p450 oxidoreductase), thereby increasing ferroptosis sensitivity. Consequently, alterations in iron metabolism, including processes, such as iron uptake, storage, utilization, and release, can modulate ferroptosis sensitivity. An extensively studied example is the induction of ferritinophagy, a selective form of autophagy that promotes the degradation of the iron storage protein ferritin in MEFs or pancreatic cancer cells, resulting in an increase in labile iron . This process has been demonstrated to enhance ferroptosis sensitivity in various disease models

Acute Toxicity	×	Carcinogenicity	×
Skin Irritation/Corrosion	×	Reproductivity	×
Serious Eye Damage/Irritation	×	STOT - Single Exposure	×
Respiratory or Skin sensitisation	×	STOT - Repeated Exposure	×
Mutagenicity	×	Aspiration Hazard	×
			•

Legend:

X – Data either not available or does not fill the criteria for classification

 Data available to make classification

# **SECTION 12 Ecological information**

	Endpoint	Test Duration (hr)	Species	Value	Source
Hardock's Ironvita Blood & Oxygen	Not Available	Not Available	Not Available	Not Available	Not Available
	Endpoint	Test Duration (hr)	Species	Value	Source
ammonium ferric citrate	EC50	72h	Algae or other aquatic plants	>100mg/l	2
	EC50	48h	Crustacea	>100mg/l	2
	LC50	96h	Fish	53mg/l	2
	EC10(ECx)	1680h	Crustacea	3.12mg/l	2
Legend:	Extracted fron	n 1. IUCLID Toxicity Data 2. Europe	ECHA Registered Substances - Ecotoxicologic	al Information - Aqu	atic Toxicit
		cotox database - Aquatic Toxicity Da ion Data 7. METI (Japan) - Bioconc	ata 5. ECETOC Aquatic Hazard Assessment Da entration Data 8. Vendor Data	ta 6. NITE (Japan) -	

Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.

Wastes resulting from use of the product must be disposed of on site or at approved waste sites.

**DO NOT** discharge into sewer or waterways.

# Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
	No Data available for all ingredients	No Data available for all ingredients

#### Bioaccumulative potential

Ingredient	Bioaccumulation
	No Data available for all ingredients

# Mobility in soil

Ingredient	Mobility
	No Data available for all ingredients

#### **SECTION 13 Disposal considerations**

Product / Packaging disposal	<ul> <li>Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.</li> <li>A Hierarchy of Controls seems to be common - the user should investigate: <ul> <li>Reduction</li> <li>Reuse</li> <li>Recycling</li> <li>Disposal (if all else fails)</li> </ul> </li> <li>This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. If it has been contaminated, it may be possible to reclaim the product by filtration, distillation or some other means. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.</li> <li><b>DO NOT</b> allow wash water from cleaning or process equipment to enter drains.</li> <li>It may be necessary to collect all wash water for treatment before disposal.</li> <li>In all cases disposal to sever may be subject to local laws and regulations and these should be considered first.</li> <li>Where in doubt contact the responsible authority.</li> <li>Recycle wherever possible.</li> <li>Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.</li> <li>Dispose of by: burial in a land-fill specifically licensed to accept chemical and / or pharmaceutical wastes or incineration in a licensed apparatus (after admixture with suitable combustible material).</li> <li>Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.</li> </ul>
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# **SECTION 14 Transport information**

#### Labels Required

Marine Pollutant	
HAZCHEM	Not Applicable
HAZCHEM	Not Applicable

### Land transport (ADG): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

#### Air transport (ICAO-IATA / DGR): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

#### Sea transport (IMDG-Code / GGVSee): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

# 14.7.1. Transport in bulk according to Annex II of MARPOL and the IBC code

Not Applicable

# 14.7.2. Transport in bulk in accordance with MARPOL Annex V and the IMSBC Code

Product name	Group
ammonium ferric citrate	Not Available

# 14.7.3. Transport in bulk in accordance with the IGC Code

Product name	Ship Type
ammonium ferric citrate	Not Available

# **SECTION 15 Regulatory information**

# Safety, health and environmental regulations / legislation specific for the substance or mixture

### ammonium ferric citrate is found on the following regulatory lists

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 2

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4

 $\label{eq:standard} Australia \ Standard \ for \ the \ Uniform \ Scheduling \ of \ Medicines \ and \ Poisons \ (SUSMP) \ - \ Schedule \ 5$ 

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 6

Australian Inventory of Industrial Chemicals (AIIC)

# Additional Regulatory Information

Not Applicable

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	Yes
Canada - DSL	Yes
Canada - NDSL	No (ammonium ferric citrate)
China - IECSC	Yes
Europe - EINEC / ELINCS / NLP	Yes
Japan - ENCS	No (ammonium ferric citrate)
Korea - KECI	Yes
New Zealand - NZIoC	Yes
Philippines - PICCS	Yes
USA - TSCA	Yes
Taiwan - TCSI	Yes
Mexico - INSQ	Yes
Vietnam - NCI	Yes
Russia - FBEPH	Yes
Legend:	Yes = All CAS declared ingredients are on the inventory No = One or more of the CAS listed ingredients are not on the inventory. These ingredients may be exempt or will require registration.

# **SECTION 16 Other information**

Revision Date	23/12/2022
Initial Date	13/03/2013

#### Other information

Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

The SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

#### Definitions and abbreviations

- PC TWA: Permissible Concentration-Time Weighted Average
- PC STEL: Permissible Concentration-Short Term Exposure Limit
- IARC: International Agency for Research on Cancer
- ACGIH: American Conference of Governmental Industrial Hygienists
- STEL: Short Term Exposure Limit
- TEEL: Temporary Emergency Exposure Limit。
- IDLH: Immediately Dangerous to Life or Health Concentrations
- ES: Exposure Standard
- OSF: Odour Safety Factor
- NOAEL: No Observed Adverse Effect Level
- LOAEL: Lowest Observed Adverse Effect Level
- TLV: Threshold Limit Value
- LOD: Limit Of Detection
- OTV: Odour Threshold Value
- BCF: BioConcentration Factors
- BEI: Biological Exposure Index
- DNEL: Derived No-Effect Level
- PNEC: Predicted no-effect concentration
- AIIC: Australian Inventory of Industrial Chemicals
- DSL: Domestic Substances List
- NDSL: Non-Domestic Substances List
- IECSC: Inventory of Existing Chemical Substance in China
- EINECS: European INventory of Existing Commercial chemical Substances
- ELINCS: European List of Notified Chemical Substances
- NLP: No-Longer Polymers
- ENCS: Existing and New Chemical Substances Inventory
- KECI: Korea Existing Chemicals Inventory
- NZIoC: New Zealand Inventory of Chemicals
- PICCS: Philippine Inventory of Chemicals and Chemical Substances

- TSCA: Toxic Substances Control Act
- TCSI: Taiwan Chemical Substance Inventory
- INSQ: Inventario Nacional de Sustancias Químicas
- NCI: National Chemical Inventory
- + FBEPH: Russian Register of Potentially Hazardous Chemical and Biological Substances

New Zealand HSNO Approval: HSR002521;

Animal Nutritional and Animal Care Products Group Standard 2017