Dihydroergotoxine mesylate

sc-203921

Material Safety Data Sheet



The Busin is Obertic

Hazard Alert Code Key: EXTREME HIGH MODERATE LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

Dihydroergotoxine mesylate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

HEALTH AZARD INST BLITY

SUPPLIER

Santa Cruz Biotechnology, Inc. 2145 Delaware Avenue Santa Cruz, California 95060 800.457.3801 or 831.457.3800

EMERGENCY:

ChemWatch

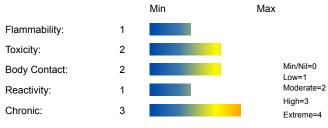
Within the US & Canada: 877-715-9305 Outside the US & Canada: +800 2436 2255 (1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

"C31-H41-N5-O5.C-H4-O3-S: C35-H41-N5-O5.C-H4-O3-S: C32-H43.N5-O5.C-", H4-O3-S, "a mixture in equal proportions of", "dihydroergocornine mesylate, dihydroergocristine mesylate and", "dihydroergocryptine mesylate (alpha-and beta-forms) 1.5:2.5:1", "dihydroergotoxine mesilate", "dihydroergotoxine mesylate", "dihydroergotoxine methanesulphonate", "dihydroerotoxin mesylate", "dihydrogenated ergot alkaloids", "ergotoxine, dihydro-, monomethanesulfonate", CCK-179, Circanol, "CO-Dergocrine mesylate", "Codergocrine Mesylate", Coristin, Dacoren, DCCK, Deapril-ST, DH-Ergotoxin-forte, Dulcion, Ergodilat, Ergoplus, Hydergin, Hydergine, Ischelium, Niloric, Optamine, Perenan, Progeril, Redergam, Segolan, Secatoxin, Redergin, "ergot alkaloid"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS





CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

Harmful if swallowed.

May cause harm to the unborn child.

Possible risk of impaired fertility.

Irritating to eyes, respiratory system and skin.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.
- Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.
- The ergot alkaloids are a group of biogenic amines which act as agonists on alpha-type adrenergic receptors. Symptoms of acute poisoning due to ergot are attributable to central system stimulation and include nausea, vomiting, diarrhoea, thirst, coldness of the skin, pruritus, weak pulse, numbness and tingling of the extremities, tachycardia, mydriasis, confusion and unconsciousness. Certain factors may predispose individuals to ergotism these may include Vitamin A and/or C deficiency, malnutrition, hepatic and renal disease and sepsis. Consumption of contaminated grain and grain products, containing ergot alkaloids, has produced poisoning of epidemic proportions and still occurs. Intense peripheral vasoconstriction of the extremities may produce gangrene and has inspired the name "St. Anthony's fire". Two forms of epidemic toxicity have been described these rarely occur together.
- A gangrenous form is characterised by agonising pain in the extremities followed by dry gangrene of the peripheral parts. Initial signs and symptoms include calf pain, cool extremities and paraesthesias (especially of the extremities). Anginal pain may be elicited in those with coronary insufficiency. Foot drop and transient monocular blindness may also occur.
- · A rarer nervous type of epidemic toxicity described as "convulsive syndrome" gives rise to paroxysmal eleptiform convulsions. Other symptoms include vertigo, headache, tinnitus, sensual disturbances, hallucinations, muscle spasm, gastrointestinal upset and convulsions. Ergotamine, a member of the group, is a potent oxytocic, producing abortion or foetal harm in pregnant women. In large repeated doses ergotamine produces all the symptoms of ergot poisoning; fatalities have occurred. Different ergot alkaloids and their derivatives have varying degrees of alpha-adrenergic blocking activity; dihydrogenated alkaloids are potent blocking agents while compounds which lack a polypeptide side-chain in their structure possess little activity.

However, it is now accepted that the varied and complex pharmacology of these alkaloids derives from their actions as partial agonists and antagonists at dopamine and serotonin receptors as well as alpha-adrenoreceptors. The most important effects are due to actions on the central nervous system and direct stimulation of the smooth muscle of the uterus and blood vessels. Differences between individual compounds may be, in part, due to varying effects at different receptors whilst the range of effects may also be dose-dependent; the physiological state of the individual may also be a factor the expression of these effects.

NOTE: The levo-isomer of the ergot alkaloids (names ending in "ine" versus "inine") is generally the highly active form.

FYF

■ This material can cause eye irritation and damage in some persons.

SKIN

- \blacksquare This material can cause inflammation of the skin on contact in some persons.
- The material may accentuate any pre-existing dermatitis condition.
- \blacksquare Open cuts, abraded or irritated skin should not be exposed to this material.
- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

- The material can cause respiratory irritation in some persons. The body's response to such irritation can cause further lung damage.
- Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.
- Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material. Ample evidence from experiments exists that there is a suspicionthis material directly reduces fertility.

There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

There is some evidence that inhaling this product is more likely to cause a sensitization reaction in some persons compared to the general population.

Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of

appropriate studies with similar materials using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

<q/>

Chronic "ergotism" (resulting from therapeutic overdose) produces circulatory disturbances due to vasoconstriction and formation of thrombi. Initial symptoms include coldness of the skin, severe muscle pain, and vascular stasis resulting in dry peripheral gangrene. Anginal pain, bradycardia and hypotension or hypertension, may also occur. Other signs include headache, nausea, vomiting, diarrhoea, dizziness, weakness of the legs, miosis, confusion, drowsiness, paralysis of one side of the body (hemiplegia) and convulsions. Interaction with the 5-HT2B serotonin receptors of cardiac myocytes, may cause proliferative heart valve disease.

Alkyl-substituted sulfonates are thought to induce genetic mutations in cells.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS				
NAME	CAS RN %			
dihydroergotoxine methanesulfonate	8067-24-1 >98			
being a mixture of				
dihydroergocornine methanesulfonate	14271-04-6			
dihydroergocristine methanesulfonate	24730-10-7			
alpha-dihydroergocryptine methanesulfonate	14271-05-7			
beta-dihydroergocryptine methanesulfonate	65914-79-6			

Section 4 - FIRST AID MEASURES

SWALLOWED

· IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY. · Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN

■ Treat symptomatically.

Ergot alkaloids are incompletely absorbed from the gastrointestinal tract and are probably metabolised in the liver. They are mainly excreted in the bile with small amounts appearing in the urine. For acute ergot intoxication:

- · the stomach should be emptied by aspiration and lavage.
- amyl nitrate inhalations may be given.
- \cdot nausea and vomiting may be controlled by intramuscular injections of 25-50 mg chlorpromazine or a comparable dose of a related phenothiazine.

MARTINDALE: The Extra Pharmacopoeia, 27th Ed.

Peripheral and coronary vasoconstriction due to ergot alkaloids may be antagonised by nitrites or papaverine and short acting barbiturates are indicated. Administration of sodium nitroprusside, anti-coagulants and dextran, with continuous monitoring of blood pressure, proved beneficial in one case of overdose due to misuse of ergotamine. GOSSELIN, SMITH HODGE: Clinical Toxicology of Commercial Products, 5th Ed.

Caffeine increase the rate and completeness of intestinal absorption of ergot alkaloids, perhaps by increasing the dissolution rate in the alkaline pH of the intestine. ELLENHORN, M.J., and Barceloux D.G.; Medical Toxicology - Diagnosis and Treatment of Human Poisoning.

Section 5 - FIRE FIGHTING MEASURES			
Vapour Pressure (mmHG):	Negligible		
Upper Explosive Limit (%):	Not available		
Specific Gravity (water=1):	Not available		
Lower Explosive Limit (%):	Not available		

EXTINGUISHING MEDIA

- · Water spray or fog.
- · Foam.

FIRE FIGHTING

- · Alert Emergency Responders and tell them location and nature of hazard.
- · Wear full body protective clothing with breathing apparatus.

When any large container (including road and rail tankers) is involved in a fire, consider evacuation by 800 metres in all directions.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- · Combustible solid which burns but propagates flame with difficulty.
- · Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO2), nitrogen oxides (NOx), sulfur oxides (SOx), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

FIRE INCOMPATIBILITY

■ Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids,chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- · Clean up waste regularly and abnormal spills immediately.
- · Avoid breathing dust and contact with skin and eyes.
- · Wear protective clothing, gloves, safety glasses and dust respirator.
- · Use dry clean up procedures and avoid generating dust.
- · Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- · Dampen with water to prevent dusting before sweeping.
- · Place in suitable containers for disposal.

MAJOR SPILLS

- · Clear area of personnel and move upwind.
- · Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

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

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- \cdot Do NOT cut, drill, grind or weld such containers.
- · In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container.
- · Lined metal can, Lined metal pail/drum
- · Plastic pail.

For low viscosity materials

- · Drums and jerricans must be of the non-removable head type.
- \cdot Where a can is to be used as an inner package, the can must have a screwed enclosure.

STORAGE REQUIREMENTS

- · Store in original containers.
- \cdot Keep containers securely sealed.

Heat and light-sensitive.

NOTE: Store in the dark.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

dihydroergotoxine methanesulfonate: CAS:8067-24-1
 dihydroergocornine methanesulfonate: CAS:14271-04-6
 dihydroergocristine methanesulfonate: CAS:24730-10-7
 alpha-dihydroergocryptine methanesulfonate: CAS:14271-05-7
 beta-dihydroergocryptine methanesulfonate: CAS:65914-79-6

PERSONAL PROTECTION









RESPIRATOR

Particulate

Consult your EHS staff for recommendations

FYF

- For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:
- · Chemical goggles
- · Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- · Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens 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].

HANDS/FEET

- Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:
- · frequency and duration of contact,
- · chemical resistance of glove material,
- · glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- · When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- · When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- · Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- · Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- · Double gloving should be considered.
- · PVC gloves.
- · Protective shoe covers.
- · Head covering.

OTHER

- \cdot For quantities up to 500 grams a laboratory coat may be suitable.
- · For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- $\cdot \ \text{For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.}$
- $\cdot \ \, \text{For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.}$
- · Eve wash unit.
- \cdot Ensure there is ready access to an emergency shower.
- · For Emergencies: Vinyl suit.

ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Mixes with water.

State	Divided solid	Molecular Weight	Not applicable
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	4.2-5.2 (0.5% sol)
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available	Specific Gravity (water=1)	Not available

Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not available

APPEARANCE

White to yellowish-white, odouress powder; mixes with water (1:50), alcohol (1:30), acetone (1:10); chloroform (1:100).

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- · Presence of incompatible materials.
- · Product is considered stable.

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

DIHYDROERGOTOXINE METHANESULFONATE

TOXICITY AND IRRITATION

- unless otherwise specified data extracted from RTECS Register of Toxic Effects of Chemical Substances.
- Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. 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. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

ALPHA-DIHYDROERGOCRYPTINE METHANESULFONATE:

BETA-DIHYDROERGOCRYPTINE METHANESULFONATE:

DIHYDROERGOCORNINE METHANESULFONATE:

■ No significant acute toxicological data identified in literature search.

DIHYDROERGOTOXINE METHANESULFONATE:

TOXICITY	IRRITATION
Oral (rat) LD50: >1000 mg/kg	Nil Reported
Intraperitoneal (rat) LD50: 500 mg/kg	
Subcutaneous (rat) LD50: >2000 mg/kg	
Intravenous (rat) LD50: >2000 mg/kg	
Intravenous (rat) LD50: 86 mg/kg	
Oral (mouse) LD50: >1 mg/kg	
Intraperitoneal (mouse) LD50: 350 mg/kg	
Subcutaneous (mouse) LD50: >4000 mg/kg	
Intravenous (mouse) LD50: 180 mg/kg	
Oral (rabbit) LD50: >1000 mg/kg	
Intravenous (rabbit) LD50: >1000 mg/kg	

■ NOTE: Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA.

Effects on newborn recorded.

TOXICITY IRRITATION

DIHYDROERGOCRISTINE METHANESULFONATE:

Oral (rat) LD50: 2643 mg/kg Nil Reported

Intravenous (rat) LD50: 91 mg/kg Oral (mouse) LD50: 2500 mg/kg

Intraperitoneal (mouse) LD50: 120 mg/kg

Intravenous (mouse) LD50: 70 mg/kg

Oral (dog) LD50: 1250 mg/kg

General anaesthesia, tremor, convulsions, nausea, vomiting recorded.

Section 12 - ECOLOGICAL INFORMATION

This material and its container must be disposed of as hazardous waste.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

| Puncture containers to prevent re-use and bury at an authorized landfill.

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.

A Hierarchy of Controls seems to be common - the user should investigate:

- · Reduction
- · Reuse
- · Recycling
- · Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. 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.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- · Recycle wherever possible.
- · Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

DOT:

Symbols: None Hazard class or Division: 6.1 Identification Numbers: UN1544 PG: III Label Codes: 6.1 Special provisions: IB8, IP3,

T1, TP33

Packaging: Exceptions: 153 Packaging: Non- bulk: 213 Packaging: Exceptions: 153 Quantity limitations: 100 kg

Passenger aircraft/rail:

Quantity Limitations: Cargo 200 kg Vessel stowage: Location: A

aircraft only:

Vessel stowage: Other: None

Hazardous materials descriptions and proper shipping names: Alkaloids, solid, n.o.s. or Alkaloid salts, solid, n.o.s. poisonous

Air Transport IATA:

ICAO/IATA Class: 6.1 ICAO/IATA Subrisk: None UN/ID Number: 1544 Packing Group: III

Special provisions: A3

Cargo Only

Packing Instructions: 619 Maximum Qty/Pack: 200 kg

Passenger and Cargo Passenger and Cargo

Packing Instructions: 619 Maximum Qty/Pack: 100 kg

Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity

Packing Instructions: Y619 Maximum Qty/Pack: 10 kg

Shipping Name: ALKALOID SALTS, SOLID, N.O.S. *(CONTAINS

DIHYDROERGOTOXINE METHANESULFONATE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None UN Number: 1544 Packing Group: III

EMS Number: F-A, S-A Special provisions: 43 223 274

Limited Quantities: 5 kg

Shipping Name: ALKALOIDS, SOLID, N.O.S. or ALKALOIDS SALTS, SOLID, N.O.S.

Section 15 - REGULATORY INFORMATION

Regulations for ingredients

dihydroergocornine methanesulfonate (CAS: 14271-04-6) is found on the following regulatory lists;

"Canada Domestic Substances List (DSL)"

dihydroergocristine methanesulfonate (CAS: 24730-10-7) is found on the following regulatory lists; "Canada Domestic Substances List (DSL)"

alpha-dihydroergocryptine methanesulfonate (CAS: 14271-05-7) is found on the following regulatory lists; "Canada Domestic Substances List (DSL)"

No data for dihydroergotoxine methanesulfonate (CAS: , 8067-24-1)

No data for beta-dihydroergocryptine methanesulfonate (CAS: , 65914-79-6)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Inhalation may produce health damage*.
- Cumulative effects may result following exposure*.
- Limited evidence of a carcinogenic effect*.
- Possible respiratory sensitiser*.
- Exposure may produce irreversible effects*.
- * (limited evidence).

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- 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.

 A list of reference resources used to assist the committee may be found at:

 www.chemwatch.net/references.
- The (M)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.

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