Juglone



Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.



SUPPLIER

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SYNONYMS

"natural product", C10-H6-O3, "1, 4-naphthoquinone, 5-hydroxy-", 5-hydroxynaphthoquinone, "5-hydroxy-1, 4-naphthoquinone", "1, 4-naphthalenedione, 5-hydroxy-", "5-hydroxy-1, 4-naphthalenedione", "1, 4-naphthoquinone, 8-hydroxy", "8-hydroxy-1, 4-naphthoquinone", "C.I. 75500", "C.I. Natural Brown 7", luglon, juglane, lawsone, nucin, "Oil red BS", regianin, "extract of juglandaceae", walnut, pecan, sedative, anti-fungal, "lawsone isomer"





EMERGENCY OVERVIEW

RISK

Toxic if swallowed. May cause SENSITISATION by skin contact. Limited evidence of a carcinogenic effect. Irritating to eyes, respiratory system and skin. Very toxic to aquatic organisms.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Toxic effects may result from the accidental ingestion of the material; animal experiments indicate that ingestion of less than 40 gram may be fatal or may produce serious damage to the health of the individual.

EYE

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

SKIN

■ This material can cause inflammation of the skin oncontact in some persons.

- The material may accentuate any pre-existing dermatitis condition.
- 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 produce serious damage 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.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. There has been concern that this material can cause cancer or mutations, but there is not enough data to make an assessment.

Skin contact with the material is more likely to cause a sensitization reaction in some persons compared to the general population.

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

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.

Quinones may undergo a reduction reaction giving rise to a semiquinone free radical. Semiquinone metabolites are highly reactive and may interact with biological macromolecules through covalent binding. They can also transfer an electron onto molecular oxygen producing superoxide radical anions, hydrogen peroxide and other reactive oxygen species. During this reaction, the quinone is regenerated and may undergo further enzyme-catalysed one-electron reduction. A reaction cycle is continuously activated - a "redox cycle".

Quinones may be produced from benzene, polycyclic aromatic hydrocarbons, estrogens, and catecholamines and give rise to reactive oxygen species that can damage DNA and other cellular macromolecules and activate signaling pathways. These molecular events may be associated with the initiation, promotion, and progression of carcinogenesis

The capacity of quinone derivatives to produce free radicals is largely influenced by the substituents on the molecule which in turn determine the efficiency of one electron reduction to semiquinone metabolites.

Oxygen activation (generation of a superoxide) occurs during one of the reactions of this metabolic sequence. Superoxide is a strong base and can therefore attract protons from a variety of compounds; it is also a potent reducing agent which can reduce transition metal ions (such as Fe3+ and Cu+) to their reduced form Superoxide may also act as a nucleophile and may readily react with a number of electrophilic agents. Finally superoxide may initiate oxidation reactions, for example, of molecules such as ascorbic acid or epinephrine (adrenaline) following hydrogen abstraction due to its basicity.

Under certain conditions the rate of formation of reactive oxygen species may exceed the capacity of the bodies auto-oxidative defence mechanisms and, as a result, result in "oxidative stress". Oxidative stress appears to be involved in some biological processes such as aging and inflammation reactions and is thought to play a role in the pathogenesis of several diseases, including acute pancreatitis, post-ischaemic syndrome,tumour formation, atherosclerosis and diabetic angiopathy.

Free radicals can react with specific cellular molecules including low molecular weight biomolecules such as neurotransmitters and co-enzymes and, as a consequence, inactivate them. macromolecules and cellular membranes are particularly vulnerable to free radical damage with the resultant loss of physiological function and cell death Depolymerisation of polysaccharides (such as hyaluronic acid) may result in inflammation of the joints.

Free radicals have a high affinity for sulfur containing amino-acids and therefore many proteins. The may bind covalently to these proteins leading to loss, of biological function such as catalysis exhibited by enzymes. Covalent binding may also result in allergic reactions when the modified protein is recognised, by the bodies immune system, as "foreign" Free radicals are also capable of causing proteins to cross-link to yield larger aggregates.

Free radicals are also able to react with the nucleic acids of DNA which may affect cell division or cell death Oxidative modifications of DNA may result in tumour initiation.

Lipids containing several double bonds (such as polyunsaturated fatty acids and cholesterol) are also subject to damage. In the case of

membrane phospholipids, such "peroxidation" results in impairment of cellular and/ or subcellular membranes which may produce cell death. Transition metal ions may also play an important role in lipid peroxidation after free radical-induced change of valency . Fe3+/Fe2+, copper and mercury ions, as well as vanadate and chromate ions seem to initiate this process and may even exacerbate it by producing secondary radicals when the phospholipid is modified.

The material may inhibit protein kinase. This family of kinases enzymatically catalyses the phosphorylation of protein . Because phosphorylation triggers a signaling cascade which in turn produces cell growth, inhibition effectively retards the process. There are several different inhibitors which act in this manner but most common are genistein (a naturally occurring steroid-like substance from soybeans), lavendustin (a microbial metabolite) and the tyrphostins (synthetic analogues).

Two families of protein kinase have been identified;

• serine-threonine kinases (also known as PKC) require calcium ion for their activation. The activated PKC phosphorylates proteins of the cellular signal cascade, which eventually induce expression of growth regulatory genes.

tyrosine kinases which similarly regulate signal transmission to growth regulatory genes

Inhibition may suppress cell or tissue growth or development.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS				
NAME		CAS RN	%	
juglone		481-39-0	>98	

Section 4 - FIRST AID MEASURES

SWALLOWED

 \cdot Give a slurry of activated charcoal in water to drink. NEVER GIVE AN UNCONSCIOUS PATIENT WATER TO DRINK. \cdot At least 3 tablespoons in a glass of water should be given.

EYE

■ If this product comes in contact with the eyes: • Immediately hold eyelids apart and flush the eye continuously with 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.

for poisons (where specific treatment regime is absent):

-----BASIC TREATMENT

· Establish a patent airway with suction where necessary.

· Watch for signs of respiratory insufficiency and assist ventilation as necessary.

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

· Foam.

· Dry chemical powder.

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), 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: Chemical goggles. 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.
- \cdot 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

- · 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.

· 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

- · Lined metal can, Lined metal pail/drum
- · Plastic pail.
- For low viscosity materials
- · Drums and jerricans must be of the non-removable head type.
- · Where a can is to be used as an inner package, the can must have a screwed enclosure.

All inner and sole packagings for substances that have been assigned to Packaging Groups I or II on the basis of inhalation toxicity criteria, must be hermetically sealed.

STORAGE REQUIREMENTS

· Store in original containers.

· Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³	Peak ppm	Peak mg/m³	TWA F/CC	Notes
US - California Permissible Exposure Limits for Chemical Contaminants	juglone (Particulates not otherwise regulated Respirable fraction)		5						(n)
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	juglone (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances	juglone (Particulates not otherwise regulated		5						

Table Z1 Limits for Air Contaminants	(PNOR)(f)- Respirable fraction)		
US - Michigan Exposure Limits for Air Contaminants	juglone (Particulates not otherwise regulated, Respirable dust)	5	
Canada - Prince Edward Island Occupational Exposure Limits	juglone (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)	10	See Appendix B current TLV/BEI Book

ENDOELTABLE

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

· Safety glasses with side shields.

· Chemical goggles.

HANDS/FEET

■ Wear chemical protective gloves, eg. PVC.

NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.

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.

OTHER

· Overalls.

· Eyewash unit.

ENGINEERING CONTROLS

· Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.

· Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid. Does not mix with water.			
State	Divided solid	Molecular Weight	174.16
Melting Range (°F)	311 (sublimes)	Viscosity	Not available
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not available
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 applicable

APPEARANCE

Does not mix well with water. Soluble in chloroform, benzene, alcohol and ether. Aqueous solutions of alkalies are purplish-red. Volatilises with steam. Isomer of lawsone

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

JUGLONE

TOXICITY AND IRRITATION

JUGLONE:

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances. TOXICITY

Oral (rat) LD50: 112 mg/kg	Nil Reported

Oral (mouse) LD50: 2.5 mg/kg

Intraperitoneal (mouse) LD50: 25 mg/kg

Intravenous (Dog) LD: 10 mg/kg

Oral (Mouse) LD50: 2.5 mg/kg

■ 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.

Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's edema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type.

Biologically active naphthoquinones readily pass through the cellular membranes where their electrophilicity enables them to conjugate with other compounds. This reaction has been implicated in the toxicity of quinones. Nucleophilic targets include thiol groups which results in inhibition of enzymes such as parvulin-like peptidyl-prolyl cis/trans isomerases, glutathione-S-transferase and cardiac sarcoplasmic reticulum Ca2+ ATPase

The toxicity of quinone compounds has been extensively studied and is generally accepted to be a function of (a) the capacity of quinones to produce oxygen free radicals and (b) the electrophilicity of quinones, which enables them to form adducts to cellular macromolecules. In vitro experiments designed to examine the relative rates of enzymatic single-electron reduction demonstrated that naphthoquinones, especially juglone, undergo rapid single-electron reduction.

Unsubstituted naphthoquinones generally do not show mutagenicity in the Salmonella mutation assay in the presence or absence of S-9 metabolic activation. However, substituted naphthoquinones containing one or more hydroxyl groups

and/or methoxyl groups have been shown to be mutagenic in S. typhimurium in the presence of S-9.

Mouse mutagen

Neoplastic by RTECS criteria

According to the German Commission E monograph on walnut hull, the topical, daily use of juglone-containing preparations of walnut bark is tied to an increased occurrence of cancer of the tongue and leukoplakia of the lips.

Dogs administered juglone intravenously (iv) at 5 mg/kg developed visible hemorrhages in the lungs, most likely related to increased capillary permeability. Since there were no significant changes in EKG, heart rate, or blood pressure, juglone did not appear to have a direct effect on the cardiovascular system.

Genotoxicity. Juglone has been tested for mutagenicity, chromosomal damage, and DNA damage in several standard assays.

A strong mutagenic response was obtained in the sex-linked recessive lethal test in adult male Drosophila melanogaster. Brood size was reduced significantly, suggesting some degree of toxicity. Because juglone is very toxic to Drosophila larvae, the larval stages were not suitable for testing mutagenic activity.

Researchers have used the w/w+ somatic mutation and recombination test (SMART) of Drosophila melanogaster to evaluate the

genotoxicity of reactive oxygen species inducers. Juglone was positive in this assay, producing a high relative value of genotoxic activity as evidenced by the increased percentage of mosaic eye progeny produced.

Tumor Promoting Activity. Juglone promoted 7,12-dimethylbenz[a]anthracene (DMBA)- initiated skin carcinomas and papillomas in Sencar mice when applied dermally at 440, 880 or 1760 nmol/mouse once a week for 40 weeks. Tumor incidence and tumor multiplicity were both dose dependent. Several other structurally related quinones were also examined, and a good correlation between the ability to induce epidermal ornithine decarboxylase and the ability to behave as a tumor promoter was noted.

Juglone promoted skin tumors in female ICR/Ha Swiss mice (30 per group) pretreated with a subcarcinogenic dose of DMBA followed by dermal application of juglone at 62 ug 3x/week for 52 weeks. Skin tumors were not observed in mice treated with the same regimen of juglone but not pre-treated with the initiator

Section 12 - ECOLOGICAL INFORMATION

Very toxic to aquatic organisms.

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

Avoid release to the environment.

Refer to special instructions/ safety data sheets.

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
juglone	LOW		LOW	HIGH

GESAMP/EHS COMPOSITE LIST - GESAMP Hazard Profiles

Name / EHS TRN A1a A1b A1 A2 B1 B2 C1 C2 C3 D1 D2 D3 E1 E2 E3 Cas No / RTECS No ________ Poly(2+)c 224 574 4 4 NR (4) NI (1) (1) (2) (1) (1) CM S 3 yclic 6 aromatics / CAS:481- 39- 0 /

Legend: EHS=EHS Number (EHS=GESAMP Working Group on the Evaluation of the Hazards of Harmful Substances Carried by Ships) NRT=Net Register Tonnage, A1a=Bioaccumulation log Pow, A1b=Bioaccumulation BCF, A1=Bioaccumulation, A2=Biodegradation, B1=Acuteaquatic toxicity LC/ECIC50 (mg/l), B2=Chronic aquatic toxicity NOEC (mg/l), C1=Acute mammalian oral toxicity LD50 (mg/kg), C2=Acutemammalian dermal toxicity LD50 (mg/kg), C3=Acute mammalian inhalation toxicity LC50 (mg/kg), D1=Skin irritation & corrosion, D2=Eye irritation & corrosion, D3=Long-term health effects, E1=Tainting, E2=Physical effects on wildlife & benthic habitats, E3=Interference with coastal amenities, For column A2: R=Readily biodegradable, NR=Not readily biodegradable. For column D3: C=Carcinogen, M=Mutagenic, R=Reprotoxic, S=Sensitising, A=Aspiration hazard, T=Target organ systemic toxicity, L=Lunginjury, N=Neurotoxic, I=Immunotoxic. For column E1: NT=Not tainting (tested), T=Tainting test positive. For column E2: Fp=Persistent floater, F=Floater, S=Sinking substances. The numerical scales start from 0 (no hazard), while higher numbers reflect increasing hazard. (GESAMP/EHS Composite List of Hazard Profiles - Hazard evaluation of substances transported by ships)

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: UN2811 PG: II Label Codes: 6.1 Special provisions: IB8, IP2, IP4. T3. TP33 Packaging: Exceptions: 153 Packaging: Non- bulk: 212 Packaging: Exceptions: 153 Quantity limitations: 25 kg Passenger aircraft/rail: Quantity Limitations: Cargo 100 kg Vessel stowage: Location: B aircraft only: Vessel stowage: Other: None Hazardous materials descriptions and proper shipping names: Toxic solids, organic, n.o.s. Air Transport IATA: ICAO/IATA Class: 6.1 ICAO/IATA Subrisk: None UN/ID Number: 2811 Packing Group: II Special provisions: A3 Cargo Only Packing Instructions: 615 Maximum Qty/Pack: 100 kg Passenger and Cargo Passenger and Cargo Packing Instructions: 613 Maximum Qty/Pack: 25 kg Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity Packing Instructions: Y613 Maximum Qty/Pack: 1 kg Shipping Name: TOXIC SOLID, ORGANIC, N.O.S. *(CONTAINS JUGLONE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None UN Number: 2811 Packing Group: II EMS Number: F-A , S-A Special provisions: 274 Limited Quantities: 500 g Marine Pollutant: Yes Shipping Name: TOXIC SOLID, ORGANIC, N.O.S.

Section 15 - REGULATORY INFORMATION

juglone (CAS: 481-39-0) is found on the following regulatory lists;

"Canada Domestic Substances List (DSL)"

Section 16 - OTHER INFORMATION

ND

Substance CAS Suggested codes juglone 481- 39- 0

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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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