(R)-(-)-Apomorphine hydrochloride

sc-203675

Material Safety Data Sheet

Hazard Alert Code Key: EXTREME | HIGH | MODERATE | LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
(R)-(-)-Apomorphine hydrochloride

STATEMENT OF HAZARDOUS NATURE
CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA


SUPPLIER
Santa Cruz Biotechnology, Inc.
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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
C17-H17-N-O2.HCl, "(R)-5, 6, 6a, 7-tetrahydro-6-methyl-4H-dibenzo[de, g]-", "quinoline-10, 11-diol hydrochloride", "amorphine hydrochloride", (-)-apomorphine, "apomorphinium chloride", "(-)-apomorphinium hydrochloride", "6a-beta-aporphine-10, 11-diol, hydrochloride", "N-methylnorapomorphine hydrochloride", "6a-beta-noraporphine-10, 11-diol, methyl-, hydrochloride", "emetic/ anti-parkinsonian agent/ dopaminergic agent"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	2		
Reactivity:	1		
Chronic:	2		

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Danger of cumulative effects.
May cause SENSITISATION by inhalation and skin contact.
Harmful by inhalation, in contact with skin and if swallowed.

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.
■ Morphine and other analgesics cause nausea, vomiting, constipation, drowsiness and confusion. Urination can be difficult, and the bowel and bile ducts can spasm.
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■ Dopamine receptor agonists are pharmacological agents with diverse physical and chemical properties that share the capacity to stimulate dopamine receptors and provide an antiparkinsonian effect. Currently available dopamine agonists belong to 2 classes: ergot (bromocriptine, lisuride, pergolide, cabergoline) and non-ergot (apomorphine, ropinirole, pramipexole, rotigotine) derivatives, each having a different pharamacological profile and different affinity for the dopaminergic receptors and subtypes.
Dopamine agonists, in clinical studies and clinical experience, appear to impair the systemic regulation of blood pressure, with resulting postural hypotension, especially during dose escalation. Parkinson's disease patients, in addition, appear to have an impaired capacity to respond to a postural challenge
Acute orthostatic hypotension is a frequent adverse effect at commencement of dopamine (dopinergic) agonist (DA) therapy. DAs are increasingly used as first-line treatment of early Parkinson's disease because of the lower incidence of motor adverse effects.
Side effects caused by DAs are similar to those of levodopa, including nausea, vomiting, orthostatic hypotension, confusion, and hallucinations. Patients intolerant of one agonist may tolerate another. As is seen with all of the antiparkinsonian drugs, elderly and demented patients are much more susceptible to psychiatric side effects.
Dopamine agonists act directly on striatal dopamine receptors. Unlike levodopa, they do not require metabolic conversion to an active form, and so their effects are independent of the degenerative state of dopaminergic terminals. They can selectively stimulate subclasses of dopamine receptors, theoretically reducing the incidence of adverse effects. Dopamine agonists do not compete with circulating plasma amino acids for absorption and transport into the brain and they do not generate free radicals or induce oxidative stress It has been demonstrated that dopamine D receptor-selective agonists may protect against glutamate-induced neurotoxicity in cultured neurons
Ergot-related side effects such as Raynaud's phenomenon, erythromelalgia, and retroperitoneal or pulmonary fibrosis are uncommon with bromocriptine and pergolide, and do not occur at all with the nonergot agonists ropinirole and pramipexole. In epidemiologic studies looking at pergolide, the onset of pulmonary and/or retroperitoneal fibrosis has been found to occur an average of 2 years following the initiation of therapy. Cardiac evaluations (e.g. Echocardiogram) should be conducted periodically on all patients taking ergot DA to monitor for the development of valve abnormalities.
Dopamine receptor agonists decrease prolactin concentration. Thus, there is a potential for decreased milk production in postpartum women taking these agents. However, this is not generally considered problematic because these agents are contraindicated in women who are breast-feeding
"Non-motor" side-effects include oedema , somnolence , constipation , dizziness , hallucinations , and nausea
Frequent side-effects include:
· allergic reactions (skin rash, itching, hives, swelling of the face, lips or tongue)
· abnormal heart beat (fast, slow or irregular
· abrupt drowsiness, sleep
· anxiety, restlessness
· difficult breathing
· dizziness
· fainting spells
· hallucinations
· skin irritation, redness, swelling, or itching
· uncontrollable movements of the arms, face, hands, head, mouth shoulders, or upper body
Dopamine agonists are typically used for treating Parkinson's disease and certain pituitary tumors (prolactinoma), and may be useful for restless legs syndrome (RLS).
Dopamine agonists activate signaling pathways through the dopamine receptor and trimeric G-proteins ultimately leading to changes in gene transcription.

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result.
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SKIN
■ Skin contact with the material may be harmful; systemic effects may resultfollowing absorption.
■ The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures.
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■ 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
■ Inhalation of dusts, generated by the material, during the course of normalhandling, may be harmful.
■ The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.
■ 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.
■ Inhalation exposure may cause susceptible individuals to show change in heart beat rhythm i.e. cardiac arrhythmia. Exposures must be terminated.
■ Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.
■ Morphine and other analgesics cause nausea, vomiting, constipation, drowsiness and confusion. Urination can be difficult, and the bowel and bile ducts can spasm.
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CHRONIC HEALTH EFFECTS
■ Repeated or long-term occupational exposure is likely to produce cumulative health effects involving organs or biochemical systems.
Inhaling this product is more likely to cause a sensitization reaction in some persons compared to the general population.
Skin contact with the material 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.
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Chronic morphine poisoning or addiction causes pin-point pupils, rapid mood changes and poor social adaptation. As dependence and tolerance occurs, there is an overwhelming need to continue taking the drug or similar drugs and to increase the dose.
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Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
apomorphine hydrochloride	314-19-2	>98

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 for a narcotic analgesic. A vigorous program of symptomatic and supportive therapy has saved many victims of poisoning.
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Excessive vomiting may be stopped by administration of a narcotic antagonist such as naloxane.

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 (CO_2), hydrogen chloride, phosgene, nitrogen oxides (NOx), 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
· 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
■ Glass container.
· Packaging as recommended by manufacturer.
· Check that containers are clearly labelled.
· Tamper-proof containers.
· Polyethylene or polypropylene containers.
· Metal drum with sealed plastic liner.
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.

STORAGE REQUIREMENTS

■ NOTE: Special security requirements may be mandated under Federal/State Regulation(s).
· Store in original containers.
· Store in vault fitted with warning devices or detectors recommended by various Federal/State authorities.
· Store in vault used only for the purpose of storage of drugs of addiction.
· Vault must be locked at all times except when the materials stored therein are required.
· Keep storage area free from debris, wastes and combustibles.
· Keep dry.
· Keep containers securely sealed.
· Protect containers against physical damage.
· Check regularly for spills and leaks.
NOTE: Store in the dark.

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	apomorphine hydrochloride (Particulates not otherwise regulated Respirable fraction)		5						(n)
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	apomorphine hydrochloride (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	apomorphine hydrochloride (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)		5						
US - Michigan Exposure Limits for Air Contaminants	apomorphine hydrochloride (Particulates not otherwise regulated, Respirable dust)		5						
Canada - Prince Edward Island Occupational Exposure Limits	apomorphine hydrochloride (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
■ 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
■ 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.
· 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
· 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.
· For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
· For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
· Eye wash unit.
· 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	303.81
Melting Range (°F)	383	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	4.8 (0.3% soln)
Decomposition Temp (°F)	437	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
White or greyish-white, odourless, glistening crystals or microcrystalline powder which becomes green on exposure to light or air; mixes with water (1:50), alcohol (1:50), Aqueous solutions are colourless but readily decompose and become green on exposure to air and light. Solutions may be stabilised by addition of dilute hydrochloric acid

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY
· Presence of incompatible materials.
· Product is considered stable.

STORAGE INCOMPATIBILITY
· Avoid strong bases.
Avoid reaction with oxidizing agents.
Incompatible with iron salts, iodides, tannins.

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

Section 11 - TOXICOLOGICAL INFORMATION

APOMORPHINE HYDROCHLORIDE

TOXICITY AND IRRITATION
APOMORPHINE HYDROCHLORIDE:
■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY	IRRITATION
Intravenous (mouse) LD50: 38 mg/kg	
Intraperitoneal (mouse) LD50: 128 mg/kg	
Oral (Mouse) LD50: 300 mg/kg *	
Intraperitoneal (Mouse) LD50: 160 mg/kg *	
Intravenous (Mouse) LD50: 56 mg/kg *	

■ 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.
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Allergic reactions involving the respiratory tract are usually due to interactions between IgE antibodies and allergens and occur rapidly. Allergic potential of the allergen and period of exposure often determine the severity of symptoms.
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Attention should be paid to atopic diathesis, characterized by increased susceptibility to nasal inflammation, asthma and eczema.
Exogenous allergic alveolitis is induced essentially by allergen specific immune-complexes of the IgG type; cell-mediated reactions (T lymphocytes) may be involved. Such allergy is of the delayed type with onset up to four hours following exposure.
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.

for hemihydrate:
Anticonvulsant behaviour recorded.
* for base
Forum Products MSDS

Section 12 - ECOLOGICAL INFORMATION

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

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
apomorphine hydrochloride	HIGH		LOW	LOW

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.
Valuable substance, hold all residues for recovery. Disposal of the material must be carried out in accordance with the requirements of the relevant Federal/State Act(s) or Code(s) regulating the disposal of Drugs of Addiction.
<\p>.
· 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: UN3249 PG: III
Label Codes: 6.1 Special provisions: T1, TP33
Packaging: Exceptions: 153 Packaging: Non- bulk: 213
Packaging: Exceptions: 153 Quantity limitations: 5 kg
Passenger aircraft/rail:
Quantity Limitations: Cargo 5 kg Vessel stowage: Location: C
aircraft only:
Vessel stowage: Other: 40
Hazardous materials descriptions and proper shipping names:
Medicine, solid, toxic, n.o.s.

Air Transport IATA:

ICAO/IATA Class: 6.1 ICAO/IATA Subrisk: None
UN/ID Number: 3249 Packing Group: III
Special provisions: A3
Cargo Only
Packing Instructions: 615 Maximum Qty/Pack: 5 kg
Passenger and Cargo Passenger and Cargo
Packing Instructions: 613 Maximum Qty/Pack: 5 kg
Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity
Packing Instructions: Y613 Maximum Qty/Pack: 5 kg
Shipping Name: MEDICINE, SOLID, TOXIC, N.O.S.(CONTAINS
APOMORPHINE HYDROCHLORIDE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None
UN Number: 3249 Packing Group: III
EMS Number: F-A , S-A Special provisions: 221 223
Limited Quantities: 5 kg
Shipping Name: MEDICINE, SOLID, TOXIC, N.O.S.

Section 15 - REGULATORY INFORMATION

apomorphine hydrochloride (CAS: 314-19-2,41372-20-7) is found on the following regulatory lists;
"Canada Non-Domestic Substances List (NDSL)","US Toxic Substances Control Act (TSCA) - Inventory"

Section 16 - OTHER INFORMATION

ND

Substance CAS Suggested codes apomorphine hydrochloride 314- 19- 2 apomorphine hydrochloride 41372- 20- 7

Ingredients with multiple CAS Nos

Ingredient Name CAS apomorphine hydrochloride 314-19-2, 41372-20-7

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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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