

Vincristine

sc-338734

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

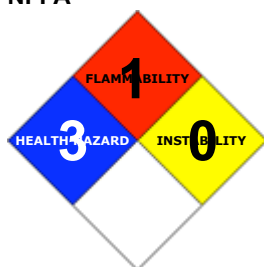
PRODUCT NAME

Vincristine

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

C46-H56-N4-O10, leurocristine, 22-oxovincalcin, 22-oxovincalbin, "vincroleukoblastine, 22-oxo-", LCR, NCI-C04864, NSC-67574, Oncovin, VCR, Vincristine, Vinkristin, "anti-cancer agent", tumoristat, tumouristat

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	3		
Body Contact:	3		
Reactivity:	1		
Chronic:	3		

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Risk of serious damage to eyes.
May cause heritable genetic damage.
Limited evidence of a carcinogenic effect.
May impair fertility.
May cause harm to the unborn child.
Harmful by inhalation, in contact with skin and if swallowed.
Irritating to 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.
- The killing action of antineoplastic drugs used for cancer chemotherapy is not selective for cancerous cells alone but affect all dividing cells. Acute side effects include loss of appetite, nausea and vomiting, allergic reaction (skin rash, itch, redness, low blood pressure, unwellness and anaphylactic shock) and local irritation.

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EYE

- If applied to the eyes, this material causes severe eye damage.

SKIN

- Skin contact with the material may be harmful; systemic effects may result following absorption.
- This material can cause inflammation of the skin on contact 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

- Inhalation of dusts, generated by the material, during the course of normal handling, may be harmful.
- The material can cause respiratory irritation in some persons. The body's response to such irritation can cause further lung damage.
- 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.
- Side effects of topoisomerase I and II inhibitors (acting as antineoplastics/ cytotoxics) include early diarrhoea which may occur within 24 hours of exposure to the drug; this may be accompanied by symptoms including runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. Late diarrhoea may occur after 24 hours and usually peaks at about 11 days after treatment. Because of concerns of dehydration and electrolyte imbalances with diarrhoea it is important to be in contact with health care professionals for monitoring, and for medication and diet modifications advice.

Other common side-effects of therapy may include nausea and vomiting may also occur; low red and white blood cell counts may also result; anaemia may follow. Hair loss, poor appetite, fever and weight loss may also ensue. Less common symptoms include constipation, shortness of breath, insomnia, cough, headache, dehydration, chills, skin rash, flatulence, flushing of the face, mouth sores, heartburn and swelling of the feet and ankles.

CHRONIC HEALTH EFFECTS

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

Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. Based on experiments and other information, there is ample evidence to presume that exposure to this material can cause genetic defects that can be inherited.

Ample evidence exists from experimentation that reduced human fertility is directly caused by exposure to the material.

Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material. Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Anti-cancer drugs used for chemotherapy can depress the bone marrow with reduction in the number of white blood cells and platelets and bleeding. Susceptibility to infections and bleeding is increased, which can be life-threatening.

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Topoisomerase inhibitors represent a subgroup of plant alkaloids, which also encompasses the vinca alkaloids such as vincristine and vinblastine, taxanes and podophyllotoxin derivatives. Topoisomerase inhibitors act by preventing the unpackaging of DNA that must occur prior to transcription and replication. The earliest drugs in this class were inhibitors of topoisomerase II, however topoisomerase I inhibitors such as topotecan started entering the market in the mid-1990's. DNA topoisomerase II inhibitors are among the most efficacious drugs for the treatment of cancer. Despite their widespread use, the use of topoisomerase II inhibitors is limited by severe adverse effects to normal tissues, including cardiotoxicity.

In addition to problems associated with toxicity, sensitivity of cancer cells to topoisomerase II targeting agents is also, like many other cancer therapeutics susceptible to resistance. The efficacy of this class is thought to depend on the expression of the topoisomerase II alpha isoform, and drug resistance is often associated with loss or mutation of this isoform.

Vinca alkaloids are toxic to the nervous system. There may be general unwellness, headache, depression, hallucinations, "pins and needles",

muscle damage, tendon reflex loss, neural inflammation of the extremities, constipation, and obstructed small bowel.

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· CAUTION: May produce immunosuppression in individuals occupationally exposed to the material.

Exposure to immunosuppressives may aggravate infectious diseases.

Chronic exposure to therapeutic doses of compounds which produce immunosuppression has been associated with development of lymphomas (occasionally malignant) and mammary tumours. These may be secondary effects induced by activation of endogenous retroviruses.

Patients on immunosuppressive medications have a 10- to 100-fold increased risk of cancer compared to the general population. Furthermore, people who currently have or have already been treated for cancer have a higher rate of tumor progression and recurrence than patients with an intact immune system.

Patients receiving immunosuppressive regimens involving combinations of drugs, as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent

Increased incidences of neoplasms, in mice and humans, have been reported after long-term immunosuppression by azathioprine and cyclosporin. Cyclosporin has been classified as a human carcinogen, by IARC, based on development of lymphomas after repeated and prolonged exposures to therapeutic doses.

Neurological and neuromuscular effects may result from treatment. Walking may be impaired as a result and neurological effects may be irreversible. These effects involve the autonomic nervous system and include malaise, headache, depression, psychoses, paraesthesia, neuromyopathy, loss of deep tendon reflexes, peripheral neuritis, constipation and adynamic ileus (inhibition of bowel movements resulting in obstruction), parotid gland pain and convulsions. Acute uric acid nephropathy (kidney damage) has occurred and alopecia (total hair loss) is common.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
vincristine	57-22-7	>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: · 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

■ For employees potentially exposed to antineoplastic and/ or cytotoxic agents on a regular basis, a preplacement physical examination and history (noting risk factors) is recommended. Periodic follow-up examinations should also be undertaken and should be overseen by a physician familiar with the toxic effects of the substance and full details of the nature of work undertaken by the employee.

After intravenous injection of vincristine it rapidly disappears from the blood and is excreted in the bile (mainly) and in the urine. Folinic acid is reported to protect mice from the lethal effects of vincristine although its use in poisoned patients must be reviewed

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), nitrogen oxides (NO_x), 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:

1. NEOPRENE

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.

It is recommended that areas handling final finished product have cytotoxic spill kits available.

Spill kits should include:

- impermeable body covering,
- shoe covers,
- latex and utility latex gloves,
- goggles,
- approved HEPA respirator,
- disposable dust pan and scoop,
- absorbent towels,
- spill control pillows,
- disposable sponges,
- sharps container,
- disposable garbage bag and
- hazardous waste label.

To avoid accidental exposure due to waste handling of cytotoxics:

- Place waste residue in a segregated sealed plastic container.
- Used syringes, needles and sharps should not be crushed, clipped, recapped, but placed directly into an approved sharps container.
- Dispose of any cleanup materials and waste residue according to all applicable laws and regulations e.g. secure chemical landfill disposal.

All personnel likely to be involved in an antineoplastic (cytotoxic) spill must receive practical training in:

- the correct procedures for handling cytotoxic drugs or waste in order to prevent and minimize the risk of spills
- the location of the spill kit in the area.

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

■ The National Institute of Health (USA) recommends that the preparation of injectable antineoplastic drugs should be performed in a Class II laminar flow biological safety cabinet and that personnel preparing drugs of this class should wear appropriate personal protective gear. Emphasise controls on containment.

- 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

■ Store in a dark glass or other suitable light resistant 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.
 - 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

- Antineoplastics (cytotoxics):
 - should be clearly identifiable to all personnel involved in their handling
 - should be stored in impervious break-resistant containers.
 - Store in original containers.
 - Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- vincristine: CAS:57-22-7

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

- Chemical protective goggles with full seal
- Shielded mask (gas-type)
- 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

- When handling antineoplastic materials, it is recommended that a disposal work-uniform (such as Tyvek or closed front surgical-type gown with knit cuffs) is worn.
- 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

■ Unless written procedures, specific to the workplace are available, the following is intended as a guide:

- For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets *; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*,
- 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.

Does not mix with water.

State	Divided solid	Molecular Weight	824.94
Melting Range (°F)	424.4- 428	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Immiscible
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 available
Volatile Component (%vol)	Negligible	Evaporation Rate	Not available

APPEARANCE

White crystalline powder; does not mix well with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

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

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

Decomposes on exposure to light.

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

Section 11 - TOXICOLOGICAL INFORMATION

VINCRIStINE

TOXICITY AND IRRITATION

VINCRIStINE:

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

TOXICITY	IRRITATION
Parental (child) LDLo: 8.29 mg/kg	Skin (rabbit): 15 mg/24h
Intravenous (child) TDLo: 0.5 mg/kg	
Intraperitoneal (rat) LD50: 1.25 mg/kg	
Intravenous (rat) LD50: 1 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.

Exposure to the material for prolonged periods may cause physical defects in the developing embryo (teratogenesis).

Equivocal tumorigen by RTECS criteria

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.

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.

- Antineoplastic (cytotoxic) wastes must be packed directly, ready for incineration, into color-coded, secure, labelled, leak-proof containers sufficiently robust to withstand handling without breaking, bursting or leaking.
- Containers of special design are available for particular needs (such as disposal of sharps) and should be used.

Section 14 - TRANSPORTATION INFORMATION

DOT:

Symbols: None Hazard class or Division: 6.1

Identification Numbers: UN1544 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: 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: 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: ALKALOID SALTS, SOLID, N.O.S. *(CONTAINS VINCRISTINE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None

UN Number: 1544 Packing Group: II

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

Limited Quantities: 500 g

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

Section 15 - REGULATORY INFORMATION

vincristine (CAS: 57-22-7) is found on the following regulatory lists;

"US - Connecticut Hazardous Air Pollutants"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.

* (limited evidence).

ND

Substance CAS Suggested codes vincristine 57- 22- 7

Germany Hazard classification and labelling of medicines with antineoplastic effects (ATC Code L01 and L02)

INN CAS Danger CMR effects CMR effects Other

Cat 1&2 Cat 3

Vinchristin 57- 22- 7 T R 46 R 60 R 61 R 20/21/22 R

36/37/38 R 41

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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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