

6-Thioguanine

sc-205587



The Power is Question

Material Safety Data Sheet

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

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

6-Thioguanine

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

C5-H5-N5-S, "2-amino-1, 7-dihydro-6H-purin-6-thione", 2-amino-6-mercaptapurine, 2-amino-6-MP, 2-aminopurine-6-thiol, 2-amino-6-purinethiol, 2-aminopurine-6(1H)-thione, BW-5071, "guanine, thio-", 6-mercapto-2-aminopurine, 6-mercaptoguanine, NSC-752, "purine-6-thiol, 2-amino-", "6-purine-6-thione, 2-amino-1, 7-dihydro-", Lanvis, Tabloid, TG, THG, Tioguanin, Tioguanine, Wellcome, U3B, X-27, "antineoplastic/ cytotoxic"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

	Min	Max	
Flammability:	1		
Toxicity:	3		
Body Contact:	2		
Reactivity:	1		
Chronic:	3		

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Toxic if swallowed.
Limited evidence of a carcinogenic effect.
May impair fertility.
May cause harm to the unborn child.
Harmful 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.
■ 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.

EYE

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

SKIN

■ The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures.
■ Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.
■ 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 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.
■ 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.

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. 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.
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.
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.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
6-thioguanine	154-42-7	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· Give a slurry of activated charcoal in water to drink. NEVER GIVE AN UNCONSCIOUS PATIENT WATER TO DRINK. · 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 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.

Incompletely and variably absorbed from the gastrointestinal tract. Activated in the body by intracellular conversion to its nucleotide, thioguanosine 5'-phosphate. About 40% of the dose is reportedly excreted in the urine within 24 hours. Does not cross the blood-brain barrier. Crosses the placenta.

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), sulfur oxides (SO_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:
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

■ 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.
- Where a can is to be used as an inner package, the can must have a screwed enclosure.

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

- 6-thioguanine: CAS:154-42-7 CAS:5580-03-0

PERSONAL PROTECTION



RESPIRATOR

Particulate

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	167.21
Melting Range (°F)	>572(decomposes)	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Immiscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
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

Pale-yellow, odourless, tasteless, crystalline powder; does not mix with water. Soluble in dilute solutions of alkali hydroxides and hot alcohol.

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

6-thioguanine

TOXICITY AND IRRITATION

6-THIOGUANINE:

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

TOXICITY	IRRITATION
Intraperitoneal (rat) LD50: 300 mg/kg	Nil Reported
Oral (mouse) LD50: 160 mg/kg	
Intraperitoneal (mouse) LD50: 54 mg/kg	
Intravenous (Cat) LD: 23.72 mg/kg	

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

for thioguanine:

Liver toxicity has been observed in a high proportion of children receiving thioguanine as part of maintenance therapy for acute lymphoblastic leukemia and in other conditions associated with continuous use of thioguanine. This liver toxicity is particularly prevalent in males. Liver toxicity usually presents as the clinical syndrome of hepatic veno-occlusive disease (hyperbilirubinemia, tender hepatomegaly, weight gain due to fluid retention, and ascites) or with signs of portal hypertension (splenomegaly, thrombocytopenia, and oesophageal varices). Histopathological features associated with this toxicity include hepatoportal sclerosis, nodular regenerative hyperplasia, peliosis hepatitis, and periportal fibrosis.

The most consistent, dose-related toxicity is bone marrow suppression. This may be manifested by anemia, leukopenia, thrombocytopenia, or any combination of these. Any one of these findings may also reflect progression of the underlying disease. Since thioguanine may have a delayed effect, it is important to withdraw the medication temporarily at the first sign of an abnormally large fall in any of the formed elements of the blood.

There are individuals with an inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) who may be unusually sensitive to the myelosuppressive effects of thioguanine and prone to developing rapid bone marrow suppression following the initiation of treatment. Substantial dosage reductions may be required to avoid the development of life-threatening bone marrow suppression in these patients.

Thioguanine may cause foetal harm when administered to a pregnant woman. Thioguanine has been shown to be teratogenic in rats when given in doses 5 times the human dose. When given to the rat on the 4th and 5th days of gestation, 13% of surviving placentas did not contain fetuses, and 19% of offspring were malformed or stunted. The malformations noted included generalized edema, cranial defects, and general skeletal hypoplasia, hydrocephalus, ventral hernia, situs inversus, and incomplete development of the limbs.

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Gastrointestinal changes, haemorrhage, effects on fertility, extra-embryonic structures recorded.

CARCINOGEN

VPVB_(VERY~	US - Maine Chemicals of High Concern List	Carcinogen
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Section 12 - ECOLOGICAL INFORMATION

Harmful to aquatic organisms.

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

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
6-thioguanine	HIGH		LOW	HIGH

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: 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: 200 kg Maximum Qty/Pack: 100 kg

Passenger and Cargo Passenger and Cargo

Packing Instructions: 677 Maximum Qty/Pack: 670

Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity

Packing Instructions: 5 kg Maximum Qty/Pack: Y645

Shipping Name: MEDICINE, SOLID, TOXIC, N.O.S.(CONTAINS 6-
THIOGUANINE)

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.

(contains 6-thioguanine)

Section 15 - REGULATORY INFORMATION

6-thioguanine (CAS: 154-42-7,5580-03-0) is found on the following regulatory lists;

"Canada Domestic Substances List (DSL)", "US - California Air Toxics ""Hot Spots"" List (Assembly Bill 2588) Substances which need not be reported unless manufactured by the facility", "US - California Proposition 65 - Priority List for the Development of MADLs for Chemicals Causing Reproductive Toxicity", "US - Maine Chemicals of High Concern List"

Section 16 - OTHER INFORMATION

ND

Substance CAS Suggested codes 6- thioguanine 154- 42- 7 T; R25 6- thioguanine 5580- 03- 0 T; R25

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

Tioguanin 154- 42- 7 T R 60 R 61 R 22 R 52

Ingredients with multiple CAS Nos

Ingredient Name CAS 6-thioguanine 154-42-7, 5580-03-0

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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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