Gliotoxin

sc-201299

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Gliotoxin

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

NFPA

SUPPLIER
Company: Santa Cruz Biotechnology, Inc.
Address:
2145 Delaware Ave
Santa Cruz, CA 95060
Telephone: 800.457.3801 or 831.457.3800
Emergency Tel: CHEMWATCH: From within the US and Canada: 877-715-9305
Emergency Tel: From outside the US and Canada: +800 2436 2255 (1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE
■ Epipolythiodioxopiperazines (ETPs) (syn: 3,6-epidithio-diketopiperazines; epi-thiodioxopiperazine) are toxic secondary metabolites made only by fungi. The best-known ETP is gliotoxin, which appears to be a virulence factor associated with invasive aspergillosis of immunocompromised patients. The toxicity of ETPs is due to the presence of a disulfide bridge, which can inactivate proteins via reaction with thiol groups, and to the generation of reactive oxygen species by redox cycling. With the availability of complete fungal genome sequences and efficient gene-disruption techniques for fungi, approaches are now feasible to delineate biosynthetic pathways for ETPs and to gain insights into the evolution of such gene clusters. Gliotoxin is an antiphagocytic and immunomodulating agent which acts by blocking membrane thiol groups. Antibiotic substance belonging to a family which includes chaetocin, sporidesmin, aranotin, and verticillin. Produced by various species of Trichodermia, Gladiocladium fimbriatum, Aspergillus fumigatus and Penicillium spp.

SYNONYMS
C13-H14-N2-O4-S2, aspergillin, "S.N. 12870", "10H, 3, 10A-epidithiopyrazino[1, 2-a]indole-1, 4-dione, ", "10H, 3, 10A-epidithiopyrazino[1, 2-a]indole-1, 4-dione, ", "2, 3, 5a, 6-hydroxy-3-(hydroxymethyl)-2-methyl-, (3R-(3alpha, 5abeta, ", "6beta, 10aalpha))-", "2, 3, 5a, 6-hydroxy-3-(hydroxymethyl)-2-methyl-, (3R-(3alpha, 5abeta, ", "6beta, 10aalpha))-", "3, 6-epidithio-2, 5-dioxopiperazine antibacterial/ antibiotic mycotoxin", "3, 6-epidithio-2, 5-dioxopiperazine antibacterial/ antibiotic mycotoxin", "antiphagocytic agent/ immunomodulating agent"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW
RISK

Toxic if swallowed.
Harmful by inhalation and in contact with skin.

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.
■ This material contains a fungal toxin. Sporidesmin A can cause facial eczema in and high levels of bile enzymes. The toxic syndrome is probably less important in humans.

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. The material may produce foreign body irritation in certain individuals.

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. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
■ 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.

CHRONIC HEALTH EFFECTS

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

- 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.
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. Prime symptom is breathlessness; lung shadows show on X-ray.
Treatment with sporidesmin A has produced some genetic aberrations and mutations. These effects are probably due to the production of free radicals.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

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

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

NAME	CAS RN	%
gliotoxin	67-99-2	>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.
- Although induction of vomiting may be recommended (IN CONSCIOUS PERSONS ONLY), such a first aid measure is dissuaded because to the risk of aspiration of stomach contents. (i) It is better to take the patient to a doctor who can

decide on the necessity and method of emptying the stomach. (ii) Special circumstances may however exist; these include non- availability of charcoal and the ready availability of the doctor.

NOTE: If vomiting is induced, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. NOTE: Wear protective gloves when inducing vomiting.

- REFER FOR MEDICAL ATTENTION WITHOUT DELAY.
- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
- If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
- If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.

(ICSC20305/20307).

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.
- Continue flushing until advised to stop by the Poisons Information Center or a doctor, or for at least 15 minutes.
- Transport to hospital or doctor without delay.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

■ If skin contact occurs:

- Immediately remove all contaminated clothing, including footwear
- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

■

- If fumes or combustion products are inhaled remove from contaminated area.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.
- Transport to hospital, or doctor.

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.
- Administer oxygen by non-rebreather mask at 10 to 15 l/min.
- Monitor and treat, where necessary, for pulmonary edema .
- Monitor and treat, where necessary, for shock.
- Anticipate seizures .
- DO NOT use emetics. Where ingestion is suspected rinse mouth and give up to 200 ml water (5 ml/kg recommended) for dilution where patient is able to swallow, has a strong gag reflex and does not drool.

ADVANCED TREATMENT

- Consider orotracheal or nasotracheal intubation for airway control in unconscious patient or where respiratory arrest has occurred.
- Positive-pressure ventilation using a bag-valve mask might be of use.
- Monitor and treat, where necessary, for arrhythmias.
- Start an IV D5W TKO. If signs of hypovolemia are present use lactated Ringers solution. Fluid overload might create complications.
- Drug therapy should be considered for pulmonary edema.
- Hypotension with signs of hypovolemia requires the cautious administration of fluids. Fluid overload might create complications.
- Treat seizures with diazepam.
- Proparacaine hydrochloride should be used to assist eye irrigation.

BRONSTEIN, A.C. and CURRANCE, P.L.
EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994.

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.
- BCF (where regulations permit).

- Carbon dioxide.
- Water spray or fog - Large fires only.

FIRE FIGHTING

■

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Use fire fighting procedures suitable for surrounding area.
- DO NOT approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

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.
- Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
- Build-up of electrostatic charge may be prevented by bonding and grounding.
- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO_2), nitrogen oxides (NOx), sulfur oxides (SOx), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.

FIRE INCOMPATIBILITY

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

PERSONAL PROTECTION

Glasses:
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

■

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

MAJOR SPILLS

■

- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Stop leak if safe to do so.
- Contain spill with sand, earth or vermiculite.
- Collect recoverable product into labeled containers for recycling.
- Neutralize/decontaminate residue.
- Collect solid residues and seal in labeled drums for disposal.
- Wash area and prevent runoff into drains.
- After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
- If contamination of drains or waterways occurs, advise emergency services.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGL) (in ppm)

AEGL 1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.
AEGL 2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.
AEGL 3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

■

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.
- DO NOT enter confined spaces until atmosphere has been checked.
- DO NOT allow material to contact humans, exposed food or food utensils.
- Avoid contact with incompatible materials.
- When handling, DO NOT eat, drink or smoke.
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling.
- Work clothes should be laundered separately.
- Launder contaminated clothing before re-use.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

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
- Polyliner drum
- Packing as recommended by manufacturer.
- Check all containers are clearly labeled and free from leaks.

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.

For materials with a viscosity of at least 2680 cSt. (23 deg. C) and solids (between 15 C deg. and 40 deg C.):

- Removable head packaging;
- Cans with friction closures and
- low pressure tubes and cartridges may be used.

- Where combination packages are used, and the inner packages are of glass, there must be sufficient inert cushioning material in contact with inner and outer packages * . - In addition, where inner packagings are glass and contain liquids of packing group I and II there must be sufficient inert absorbent to absorb any spillage *. - * unless the outer packaging is a close fitting molded plastic box and the substances are not incompatible with the plastic.

STORAGE REQUIREMENTS

■

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS

X X + X X +

X: Must not be stored together
O: May be stored together with specific preventions
+: May be stored together

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 - Oregon Permissible Exposure Limits (Z3)	gliotoxin (Inert or Nuisance Dust: (d) Total dust)		10						*
US OSHA Permissible Exposure Levels (PELs) - Table Z3	gliotoxin (Inert or Nuisance Dust: (d) Respirable fraction)		5						

US OSHA Permissible Exposure Levels (PELs) - Table Z3	gliotoxin (Inert or Nuisance Dust: (d) Total dust)	15	
US - Hawaii Air Contaminant Limits	gliotoxin (Particulates not other wise regulated - Total dust)	10	
US - Hawaii Air Contaminant Limits	gliotoxin (Particulates not other wise regulated - Respirable fraction)	5	
US - Oregon Permissible Exposure Limits (Z3)	gliotoxin (Inert or Nuisance Dust: (d) Respirable fraction)	5	*
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	gliotoxin (Particulates not otherwise regulated Respirable fraction)	5	
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	gliotoxin (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)	5	
US - Michigan Exposure Limits for Air Contaminants	gliotoxin (Particulates not otherwise regulated, Respirable dust)	5	

MATERIAL DATA

GLIOTOXIN:

■ Airborne particulate or vapor must be kept to levels as low as is practicably achievable given access to modern engineering controls and monitoring hardware. Biologically active compounds may produce idiosyncratic effects which are entirely unpredictable on the basis of literature searches and prior clinical experience (both recent and past).

PERSONAL PROTECTION




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

■ 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
- Handle extremely poisonous natural toxins in closed systems such as glove bags or other enclosures, to avoid accidental contact. Workers should wear complete disposable clothing including shoe covers, gloves and mask with an independent air supply.

■

- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
- The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
- Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory . These may be government mandated or vendor recommended.
- Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
- Use approved positive flow mask if significant quantities of dust becomes airborne.
- Try to avoid creating dust conditions.

RESPIRATOR

■

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow
Explanation of Respirator Codes:
Class 1 low to medium absorption capacity filters.
Class 2 medium absorption capacity filters.
Class 3 high absorption capacity filters.
PAPR Powered Air Purifying Respirator (positive pressure) cartridge.
Type A for use against certain organic gases and vapors.
Type AX for use against low boiling point organic compounds (less than 65ºC).
Type B for use against certain inorganic gases and other acid gases and vapors.
Type E for use against sulfur dioxide and other acid gases and vapors.
Type K for use against ammonia and organic ammonia derivatives
Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.
Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.
Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.
The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.
Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

■ For potent pharmacological agents:
Powders
To prevent contamination and overexposure, no open handling of powder should be allowed.

- Powder handling operations are to be done in a powders weighing hood, a glove box, or other equivalent ventilated containment system.
- In situations where these ventilated containment hoods have not been installed, a non-ventilated enclosed containment hood should be used.
- Pending changes resulting from additional air monitoring data, up to 300 mg can be handled outside of an enclosure provided that no grinding, crushing or other dust-generating process occurs.
- An air-purifying respirator should be worn by all personnel in the immediate area in cases where non-ventilated containment is used, where significant amounts of material (e.g., more than 2 grams) are used, or where the material may become airborne (as through grinding, etc.).
- Powder should be put into solution or a closed or covered container after handling.
- If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.

Solutions Handling:

- Solutions can be handled outside a containment system or without local exhaust ventilation during procedures with no potential for aerosolisation. If the procedures have a potential for aerosolisation, an air-purifying respirator is to be worn by all personnel in the immediate area.
- Solutions used for procedures where aerosolisation may occur (e.g., vortexing, pumping) are to be handled within a containment system or with local exhaust ventilation.
- In situations where this is not feasible (may include animal dosing), an air-purifying respirator is to be worn by all personnel in the immediate area. If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.
- Ensure gloves are protective against solvents in use.

Air should be supplied by an independent system.
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.
Barrier protection or laminar flow cabinets should be considered for laboratory scale handling.
The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated: Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated.
Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved. Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to

uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapors, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood-local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.
Does not mix with water.

State	Divided solid	Molecular Weight	326.4
Melting Range (°F)	429.8 (decomposes)	Viscosity	Not available
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
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)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not available

APPEARANCE

White crystalline powder; does not mix well with water (0.07 mg/ml, 30 C.) Solubilities (mg/ml, 7 deg. C.): acetic acid 12, acetone 9, acetonitrile 10.2, benzene 5.5, carbon tetrachloride 0.8, chloroform 20, dioxane 73 (decomposes), dimethylformamide 17, ethyl acetate 8.5, ethanol 4.7, methanol 1.4, pyridine 77. Sensitive to oxidation and heat; inactivated when heated for 10 minutes at 100 deg. C.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

■

- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

gliotoxin

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (mouse) LD50: 67 mg/kg	Nil Reported
Intraperitoneal (mouse) LD50: 32 mg/kg	

Subcutaneous (mouse) LD50: 25 mg/kg

Intravenous (mouse) LD50: 7.8 mg/kg

■ for epipolythiodioxopiperazines (ETPs); syn epi-thiodioxopiperazine; 3,6-epidithio-diketopiperazines:

ETPs are fungitoxic. Although uptake mechanisms by mammalian target cells are well described, the manner in which these compounds are exported by such cells or from the fungi that produce them has not been reported.
Gliotoxin can selectively kill activated hepatic stellate cells in rats, which is a model system for liver fibrosis. This morbidity is caused by selective induction of apoptotic cell death in stellate cells through redox-dependent effects on the adenine nucleotide transporter. However, the usefulness of ETPs such as gliotoxin as antimicrobial agents, and as clinical immunosuppressive agents, will be limited by their toxicity. Their targeting of mitochondrial function is also significant, given the importance of this organelle in triggering cell death and elicits interest in mitochondria as cellular targets in cancer therapy.
Gliotoxin appears to be a potent immunosuppressive agent in vitro with action on macrophages and antigen-presenting cells. Although in vitro studies show mixed disulphide formation with proteins, the role of mixed disulfides in the cellular toxicity of ETPs has not been established unequivocally. One target is the transcription factor NF-kB, which is inhibited in cells by gliotoxin, probably via interaction with an essential thiol residue. Since this factor is an integral part of the inflammatory immune response and controls expression of some cytokines, its inhibition may account for the immunosuppressive properties of ETPs.
Another cellular target is the mitochondrion. Mitochondrial function in intact cells is inhibited by the scabrosin ester ETP . Initially mitochondrial ATP synthase is inhibited, then the mitochondrial membrane becomes hyperpolarised, and finally apoptotic cell death occurs. Effects of gliotoxin on isolated mitochondria include release of both calcium and magnesium.
The epipolythiodioxopiperazines (ETPs), are characterised by the presence of an internal disulfide bridge . The diketopiperazine ring is derived from a cyclic dipeptide and its sulfur bridge imparts all known toxicity of these molecules. The nature of side groups of ETPs does not appear to affect toxicity. Indeed the synthetic ETP 1,4-dimethyl-3,6-epidithio-2,5- dioxopiperazine has similar toxicity to that of natural ETPs The effect of gliotoxin on animal cell cultures has been studied extensively, Removal of the sulfur atoms or addition of the reducing agent dithiothreitol completely reveres ant-viral RNA replication. Toxicity is thought to be mediated in at least two ways:

- conjugation to proteins with susceptible thiol residues and subsequent inactivation; and
- generation of reactive oxygen species via redox cycling.

However the role of these processes in toxicity is equivocal and many findings appear to be contradictory. ETPs do not have exclusive protein targets. For some proteins, the cysteine residues that form mixed disulfide bonds with ETPs have been identified.
Altered sleep time, lowered blood pressure, diarrhoea recorded.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:
GLIOTOXIN:
■ DO NOT discharge into sewer or waterways.

Ecotoxicity

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

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.
For small quantities:

- Treat a dilute basic solution (pH10-11) of the material with a50% excess of commercial laundry bleach.
- Control temperature by rate of bleach addition.
- Adjust pH if necessary.
- Stand overnight, then cautiously adjust pH to 7.
- Evolution of gas may occur.
- Filter solids for disposal to land-fill (subject to local regulation).
- Precipitate any heavy metals by addition of sulfide.
- Recycle wherever possible. Special hazard may exist - specialist advicemay be required.
- Consult manufacturer for recycling options.
- Consult Waste Management Authority for disposal.
- Bury or incinerate residue at an approved site.
- Decontaminate empty containers. Observe all label safeguards untilcontainers are cleaned and destroyed.
- Puncture containers to prevent re-use and bury at an authorized landfill.

Section 14 - TRANSPORTATION INFORMATION

DOT:

Symbols:	None	Hazard class or Division:	6.1
Identification Numbers:	UN3462	PG:	III
Label Codes:	6.1	Special provisions:	141, IB8, IP3, T1 TP33
Packaging: Exceptions:	153	Packaging: Non-bulk:	213
Packaging: Exceptions:	153	Quantity limitations: Passenger aircraft/rail:	100 kg
Quantity Limitations: Cargo aircraft only:	200 kg	Vessel stowage: Location:	A
Vessel stowage: Other:	None		

Hazardous materials descriptions and proper shipping names:
Toxins, extracted from living sources, solid, n.o.s.

Air Transport IATA:

ICAO/IATA Class:	6.1	ICAO/IATA Subrisk:	None
UN/ID Number:	3462	Packing Group:	III
Special provisions:	A3		

Shipping Name: TOXINS, EXTRACTED FROM LIVING SOURCES, SOLID, N.O.S. *(CONTAINS GLIOTOXIN)

Maritime Transport IMDG:

IMDG Class:	6.1	IMDG Subrisk:	None
UN Number:	3462	Packing Group:	III
EMS Number:	F-A,S-A	Special provisions:	210 223 274 944
Limited Quantities:	5 kg		

Shipping Name: TOXINS EXTRACTED FROM LIVING SOURCES, SOLID, N.O.S.(contains gliotoxin)

Section 15 - REGULATORY INFORMATION

gliotoxin (CAS: 67-99-2) is found on the following regulatory lists;
"US - Hawaii Air Contaminant Limits","US - Oregon Permissible Exposure Limits (Z3)","US OSHA Permissible Exposure Levels (PELs) - Table Z3"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
■ Limited evidence of a carcinogenic effect*.
* (limited evidence).

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ Classification of the mixture 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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