Altretamine

Material Safety Data Sheet

Hazard Alert Code Key: EXTREME HIGH MODERATE LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Altretamine

STATEMENT OF HAZARDOUS NATURE

NFPA

SUPPLIER
Company: Santa Cruz Biotechnology, Inc.
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
Antineoplastic agent given by mouth for treatment of ovarian carcinoma (stage III and IV) and other solid tumours. Metabolism of hexamethylmelamine is a requirement for cytotoxicity. Synthetic monohydroxymethylmelamines, and products of hexamethylmelamine metabolism, in vitro and in vivo, form covalent adducts with tissue macromolecules including DNA. Whether such adducts are responsible for antineoplastic activity is unclear. The drug bears structural similarities to the alkylating agent, triethylenemelamine, which has been shown to be carcinogenic in animals

SYNONYMS
C9-H18-N6, "melamine, hexamethyl-", "1, 3, 5-triazine-2, 4, 6-triamine, N, N, N’ N” N” -hexamethyl-", "s-triazine, 2, 4, 6-tris(dimethylamino)-", "2, 4, 6-tris(dimethylamino)s-triazine", "2, 4, 6-tris(dimethylamino)-1, 3, 5-triazine", Altretamine, ENT-50852, Hemel, Hexastat, HMM, NCI-C50259, NSC-13875, antineoplastic

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability</td>
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<td></td>
</tr>
<tr>
<td>Toxicity</td>
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<td></td>
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<tr>
<td>Body Contact</td>
<td>2</td>
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<tr>
<td>Reactivity</td>
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<td>Chronic</td>
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Days decreased spermatogenesis and atrophied testes, seminal vesicles and the ventral prostate. Aspermatogenesis, and a possible dominant lethal mutagenic effect were noted. Administration of 460-1 mg/kg/day to male rats for approximately 60 days prior to mating, testicular atrophy, reduced sperm count and decreased fertility was observed. The gestation period produced no adverse effects on fertility but did decrease post-natal survival. The development of aplastic anemia due to complete destruction of the stem cells.

Hexamethylmelamine is embryotoxic in rats (142-570 mg/kg/day) and rabbits (1040 mg/kg/day) and teratogenic in rats (570 mg/kg/day) and rabbits (1040 mg/kg/day). This 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. Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

Acute side effects include loss of appetite, nausea and vomiting, allergic reaction (skin rash, itch, redness), low blood pressure, unwellness and anaphylactic shock. 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. Gout and renal failure can occur.

Triazine derivatives have been shown to cause structural damage to the liver in animal studies. 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.

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. Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

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Chronic health effects involving organs or biochemical systems. 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.

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. Digestive system effects may include inflammation of the mouth cavity, mouth ulcers, esophagus inflammation, abdominal pain and bleeds, diarrhea, bowel ulcers and perforation. Reversible hair loss can result and wound healing may be delayed. Long-term effects on the gonads may cause periods to stop and inhibit sperm production. Most anti-cancer drugs can potentially cause mutations and birth defects, and coupled with the effects of the suppression of the immune system, may also cause cancer.

Alkylating agents may damage the stem cell which acts as the precursor to components of the blood. Loss of the stem cell may result in pancytopenia (a reduction in the number of red and white blood cells and platelets) with a latency period corresponding to the lifetime of the individual blood cells. Granulocytopenia (a reduction in granular leukocytes) develops within days and thrombocytopenia (a disorder involving platelets), within 1-2 weeks, whilst loss of erythrocytes (red blood cells) needs months to become clinically manifest. Aplastic anaemia develops due to complete destruction of the stem cells. Hexamethylmelamine is embryotoxic in rats (142-150 mg/kg/day) and rabbits (1420 mg/kg/day) and teratogenic in rats (570 mg/kg/day) and may cause foetal damage in humans. Doses of 120 mg/kg/day administered to female rats 14 days prior to breeding and through the gestation period produced no adverse effects on fertility but did decrease post-natal survival. The drug was embryocidal at 240 mg/m3/day. When administered to male rats for approximately 60 days prior to mating, testicular atrophy, reduced fertility, focal or diffuse aspermatogenesis, and a possible dominant lethal mutagenic effect were noted. Administration of 460-1800 mg/kg/day to male rats for 10 days decreased spermatogenesis and atrophied testes, seminal vesicles and the ventral prostate.
Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAS RN</th>
<th>%</th>
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<tbody>
<tr>
<td>hexamethylmelamine</td>
<td>645-05-6</td>
<td>&gt;98</td>
</tr>
</tbody>
</table>

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:
  - For advice, contact a Poisons Information Center or a doctor.
  - Urgent hospital treatment is likely to be needed.
  - If conscious, give water to drink.
  - INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

NOTE: Wear a protective glove when inducing vomiting by mechanical means.

- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as such as alcalization of 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.

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.
  - If pain persists or recurs seek medical attention.
  - 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, without delay.

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. Following administration of antineoplastics, control of nausea and vomiting may be attempted by giving phenothiazines such as perphenazine, prochlorperazine, promethazine or thiethylperazine before antineoplastic agents are administered. In bone-marrow depression, transfusion of blood or platelets reduces the risk of life-threatening hemorrhage. Granulocyte transfusions and injection of antibiotics may be necessary to combat infection in the neutropenic patient. Hyperuricemia is avoided by the addition of allopurinol to treatment schedules and measures such as alcalization of the urine and hydration may be adopted. MARTINDALE: The Extra Pharmacopeia, 28th Edition.

Plasma half-life is reported to range from 4.7 to 10.2 hours.
Hexamethylmelamine and its metabolites bind to plasma proteins. Urinary excretion is essentially complete at 72 hours. Excretory organs in mice (liver and kidney) and the small intestine show high concentrations after intraperitoneal administration.

Section 5 - FIRE FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tr>
<td>Vapour Pressure (mmHG)</td>
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<td>Upper Explosive Limit (%)</td>
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<tr>
<td>Specific Gravity (water=1)</td>
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</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not available.</td>
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</table>
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 breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- Use water delivered as a fine spray to control fire and cool adjacent 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 (CO2), nitrogen oxides (NOx), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.
May emit corrosive 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

- 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.
- 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.

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 skill kit in the area
- the arrangements for medical treatment of any affected personnel
- the procedure for containment of the spill, and decontamination of personnel and the environment, including the different procedures for major and minor spills
- the procedure for waste disposal according to the nature and extent of the spill

**MAJOR SPILLS**
- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.
- Recover product wherever possible.
- IF DRY: Use dry cleanup procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal.
- ALWAYS: Wash area down with large amounts of water and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise emergency services.

**PROTECTIVE ACTIONS FOR SPILL**

**From US Emergency Response Guide 2000 Guide No guide found.**

**From IERG (Canada/Australia)**

**FOOTNOTES**

1 PROTECTIVE ACTION ZONE is defined as the area in which people are at risk of harmful exposure. This zone assumes that random changes in wind direction confines the vapour plume to an area within 30 degrees on either side of the predominant wind direction, resulting in a crosswind protective action distance equal to the downwind protective action distance.

2 PROTECTIVE ACTIONS should be initiated to the extent possible, beginning with those closest to the spill and working away from the site in the downwind direction. Within the protective action zone a level of vapour concentration may exist resulting in nearly all unprotected persons becoming incapacitated and unable to take protective action and/or incurring serious or irreversible health effects.

3 INITIAL ISOLATION ZONE is determined as an area, including upwind of the incident, within which a high probability of localised wind reversal may expose nearly all persons without appropriate protection to life-threatening concentrations of the material.

4 SMALL SPILLS involve a leaking package of 200 litres (55 US gallons) or less, such as a drum (jerican or box with inner containers). Larger packages leaking less than 200 litres and compressed gas leaking from a small cylinder are also considered "small spills". LARGE SPILLS involve many small leaking packages or a leaking package of greater than 200 litres, such as a cargo tank, portable tank or a "one-tonne" compressed gas cylinder.

5 Guide No guide found. is taken from the US DOT emergency response guide book.

6 IERG information is derived from CANUTEC - Transport Canada.

**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

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.
- 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.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

Antineoplastics (cytotoxics):

- should be clearly identifiable to all personnel involved in their handling
- should be stored in impervious break-resistant containers
- should be stored in separate, clearly marked storage areas to minimize the risk of breakage, and to limit contamination in the event of leakage.

Spill kits should be available in storage areas.

- 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: 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

The following materials had no OELs on our records

- hexamethylmelamine: CAS:645-05-6

MATERIAL DATA

HEXAMETHYLMELAMINE:

It is the goal of the ACGIH (and other Agencies) to recommend TLVs (or their equivalent) for all substances for which there is evidence of health effects at airborne concentrations encountered in the workplace.

At this time no TLV has been established, even though this material may produce adverse health effects (as evidenced in animal experiments.
Airborne concentrations must be maintained as low as is practically possible and occupational exposure must be kept to a minimum.

NOTE: The ACGIH occupational exposure standard for Particles Not Otherwise Specified (P.N.O.S) does NOT apply.

Sensory irritants are chemicals that produce temporary and undesirable side-effects on the eyes, nose or throat. Historically occupational exposure standards for these irritants have been based on observation of workers’ responses to various airborne concentrations. Present day expectations require that nearly every individual should be protected against even minor sensory irritation and exposure standards are established using uncertainty factors or safety factors of 5 to 10 or more. On occasion animal no-observable-effect-levels (NOEL) are used to determine these limits where human results are unavailable. An additional approach, typically used by the TLV committee (USA) in determining respiratory standards for this group of chemicals, has been to assign ceiling values (TLV C) to rapidly acting irritants and to assign short-term exposure limits (TLV STELs) when the weight of evidence from irritation, bioaccumulation and other endpoints combine to warrant such a limit. In contrast the MAK Commission (Germany) uses a five-category system based on intensive odour, local irritation, and elimination half-life. However this system is being replaced to be consistent with the European Union (EU) Scientific Committee for Occupational Exposure Limits (SCOEL); this is more closely allied to that of the USA.

OSHA (USA) concluded that exposure to sensory irritants can:
- cause inflammation
- cause increased susceptibility to other irritants and infectious agents
- lead to permanent injury or dysfunction
- permit greater absorption of hazardous substances and
- acclimate the worker to the irritant warning properties of these substances thus increasing the risk of overexposure.

CEL TWA: 0.001 mg/m3.

PERSONAL PROTECTION

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 lenses 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.
Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.
  - polychloroprene
  - nitrile rubber
  - butyl rubber
  - fluorocautchoch
  - polyvinyl chloride
Gloves should be examined for wear and/or degradation constantly.

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

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 equipment. 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

<table>
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<tr>
<th>Protection Factor</th>
<th>Half-Face Respirator</th>
<th>Full-Face Respirator</th>
<th>Powered Air Respirator</th>
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<td>10 x PEL</td>
<td>P1</td>
<td>-</td>
<td>PAPR-P1</td>
</tr>
<tr>
<td>50 x PEL</td>
<td>Air-line*</td>
<td>P2</td>
<td>-</td>
</tr>
<tr>
<td>100 x PEL</td>
<td>Air-line**</td>
<td>P3</td>
<td>-</td>
</tr>
<tr>
<td>100+ x PEL</td>
<td>-</td>
<td>Air-line*</td>
<td>PAPR-P3</td>
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</table>

- * - 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 65°C).

Type B for use against certain inorganic gases and 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.

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.
- 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. When handling: Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered; Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered; Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered.

Written procedures, specific to a particular workplace, may replace these recommendations.

* For Class II Biological Safety Cabinets, Types B2 or B3 should be considered. Where only Class I, open fronted Cabinets are available, glove panels may be added, Laminar flow cabinets do not provide sufficient protection when handling these materials unless especially designed to do so.

### Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

**PHYSICAL PROPERTIES**

Solid. Does not mix with water.

<table>
<thead>
<tr>
<th>State</th>
<th>Melting Range (°F)</th>
<th>Boiling Range (°F)</th>
<th>Flash Point (°F)</th>
<th>Decomposition Temp (°F)</th>
<th>Autoignition Temp (°F)</th>
<th>Upper Explosive Limit (%)</th>
<th>Lower Explosive Limit (%)</th>
<th>Volatile Component (%vol)</th>
<th>APPEARANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divided solid</td>
<td>341.6 (+/-) 1</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Negligible</td>
<td>White crystalline powder; does not mix well with water. Increasingly soluble in water at pH 3 and below. Soluble in chloroform, ether.</td>
</tr>
</tbody>
</table>

**Molecular Weight** 210.3

**Viscosity** Not Applicable

**Solubility in water (g/L)** Partly miscible

**pH (1% solution)** Not applicable

**pH (as supplied)** Not applicable

**Vapour Pressure (mmHG)** Negligible

**Specific Gravity (water=1)** Not available

**Relative Vapor Density (air=1)** Not Applicable

**Evaporation Rate** Not applicable

### 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

*hexamethylenimine*

**TOXICITY AND IRRITATION**

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

<table>
<thead>
<tr>
<th>TOXICITY</th>
<th>IRRITATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (human) TDLo: 8 mg/kg</td>
<td>Nil Reported</td>
</tr>
<tr>
<td>Oral (rat) LD50: 350 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal (rat) LD50: 265 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>
A Hierarchy of Controls seems to be common - the user should investigate:

• their area. In some areas, certain wastes must be tracked.

• All waste must be handled in accordance with local, state and federal regulations.

Disposal Instructions:

All waste must be handled in accordance with local, state and federal regulations.

Chemical Name: Hexamethylmelamine

Use of the material will result in wastes that are toxic to aquatic life (freshwater and marine) and may have harmful effects on reproduction in fish, birds, bees and other organisms.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

HEXAMETHYLMELAMINE:

- Harmful to aquatic organisms.
- May cause long-term adverse effects in the aquatic environment.
- Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.
- Wastes resulting from use of the product must be disposed of on site or at approved waste sites.
- For antineoplastics:
  
  **Ecotoxicity:**
  
  Because antineoplastics are genotoxic, mutagenic and carcinogenic concerns are warranted for their potential effect in the environment. There are a number of known mammalian toxic and nausea effects associated with antineoplastic treatment, which could indicate that similar effects, might be expected in non-target mammals, and possibly also in non-target species other than mammals. Total dosage over a whole therapy protocol is approximately 150 mg/kg body weight. Approximately 14-53% of the administered pharmaceutical is excreted unmetabolised into urine.
  
  Antineoplastics as a class of drugs are of potential concern for environmental impacts, not just for their acute toxicity but perhaps more for their ability to effect subtle genetic changes, the cumulative impact of which over time can lead to more profound ecologic change. Hospitals are the major source of genotoxic drugs. Publicly-owned waste-water treatment works (POTWs) that serve hospitals, especially multiple hospitals, are likely candidates for releasing these chemicals into surface waters.
  
  Antineoplastics are highly [geno]toxic compounds, primarily from hospitals, with poor removal from sewage treatment plants (STWs). Antineoplastic agents, antitumour agents primarily used only within hospitals for chemotherapy, are found sporadically and in a range of concentrations, probably because only small amounts are introduced to STWs via domestic sewage because of their long-lived physiologic retention.
  
  These compounds act as nonspecific alkylating agents (i.e., specific receptors are not involved) and therefore have the potential to act as either acute or long-felt stressors (mutagens carcinogens/teratogens/embryotoxins) in any organism.
  
  Using well-established QSAR modelling techniques almost 1/5 of the commonly used antineoplastics were predicted to be very toxic to algae, and close to 1/3 were predicted to be non-toxic to plants. A third of the compounds were predicted to be very toxic to daphnids, and almost half were predicted to be non-toxic to daphnids. Slightly more than 1/5 were predicted to be very toxic to fish, and 47% were predicted to be non-toxic to fish.
  
  DO NOT discharge into sewer or waterways.

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:

• their area. In some areas, certain wastes must be tracked.

• All waste must be handled in accordance with local, state and federal regulations.

**Intravenous (mouse) LD50: 171 mg/kg**

**Intravenous (chicken) LD50: 341 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-allergic 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.

**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.

- Nausea, vomiting, leukopenia, chromodacryorrhea, haemorrhage, granulocytopenia, changes in bone marrow, cardiomyopathy, zonal hepatitis (hepatocellular necrosis), changes in leukocyte count, pigmented/nucleated red blood cells, enzyme changes, flaccid paralysis, ataxia, gastrointestinal tract changes, reproductive system tumours, leukaemia, kidney tumours, skin tumours, paternal effects, foetolethality, foetotoxicity, effects on newborn recorded

**Neoplastic by RTECS criteria. Equivocal tumourigen by RTECS criteria.**

**Refer to data for ingredients, which follows:**

**HEXAMETHYLMELAMINE:**

- Harmful to aquatic organisms.
- May cause long-term adverse effects in the aquatic environment.
- Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.
- Wastes resulting from use of the product must be disposed of on site or at approved waste sites.
- For antineoplastics:
  
  **Ecotoxicity:**
  
  Because antineoplastics are genotoxic, mutagenic and carcinogenic concerns are warranted for their potential effect in the environment. There are a number of known mammalian toxic and nausea effects associated with antineoplastic treatment, which could indicate that similar effects, might be expected in non-target mammals, and possibly also in non-target species other than mammals. Total dosage over a whole therapy protocol is approximately 150 mg/kg body weight. Approximately 14-53% of the administered pharmaceutical is excreted unmetabolised into urine.
  
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  DO NOT discharge into sewer or waterways.
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.
- Once filled and closed, such containers must never be re-opened.
- Immediate containers must bear a nationally accepted symbol or device depicting cytotoxic substances and be labelled with the words: CYTOTOXIC WASTE - INCINERATE in a style of lettering approved by the national/state authority.
- Where policies and procedures permit the merging of cytotoxic wastes with medical waste in an outer container used for medical waste, cytotoxic waste must first be placed in identifiable color-coded/labelled cytotoxic containers prior to merging.
- Management procedures must ensure that merged medical and cytotoxic waste is subjected to the incineration requirements appropriate for the total destruction of the cytotoxic waste.

WASTE STORAGE OF CYTOTOXIC WASTES For the storage of cytotoxic waste, segregated or merged with medical waste, provide:
- special storage areas with adequate lighting.
- waste security and restriction of access to authorized persons.
- storage areas designed to facilitate easy routine cleaning and maintenance to hygienic standards, or post-spill decontamination.
- storage of cytotoxic waste in standard, identifying bins or other appropriate containers.

COLLECTION OF CYTOTOXIC WASTES
- Procedures for the collection of cytotoxic wastes, which are compatible with existing operational needs, and which protect workers, other people and the environment, must be developed.
- Waste must be removed from the site by contractors whose workers have been instructed in the protective methods to be used against the hazards involved, and who comply with the safe work practices established by internal and/or national/state policies. Contractors must instruct, train and direct their personnel in the safe and legal handling of cytotoxic wastes. Contractor's personnel should observe the operating procedures of the waste-generator.
- Transport of cytotoxic wastes, through the community, must comply with the appropriate national/state codes.

DESTRUCTION OF CYTOTOXIC WASTES
- Destruction of cytotoxic wastes should be carried out in multi-chambered incinerators, licenced for this purpose, operating at 1100 deg. C. or more, with a residence time of at least 1 second.
- Operators must be trained in handling procedures and hazards involved with handling the waste.
- Waste which arrives at the incinerator inappropriately packaged should NOT be returned to the waste generator. An authorized representative of the waste generator must attend the incinerator site to rectify the situation.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

REGULATIONS

hexamethylmelamine (CAS: 645-05-6) is found on the following regulatory lists:

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
- Cumulative effects may result following exposure*.
- Limited evidence of a carcinogenic effect*.
- Exposure may produce irreversible effects*.
* (limited evidence).

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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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