**Bleomycin Safe Handling, Disposal, and Storage Procedures**

**Georgia Tech Policy Regarding the Purchase and Use of Antineoplastic Agents**

- Any use of antineoplastic agents involving vertebrate animals must be pre-approved by the Georgia Tech Institute Animal Care and Use Committee (IACUC).

- It is the Principle Investigator’s responsibility to communicate any intended use of any antineoplastic agent to the Georgia Tech Laboratory and Chemical Safety Manager, Deborah Wolfe-Lopez, (Debbie.wolfe-lopez@ehs.gatech.edu) prior to the purchase of the material.

- Any intended use of antineoplastic agents involving vertebrate animals must also be communicated to the Director of the Georgia Tech Physiology Research Center, Dr. Laura O’Farrell (laura.ofarrell@gtrc.gatech.edu), prior to the acquisition of the animals.

**Bleomycin**

Bleomycin is a mixture of cytotoxic glycopeptide antibiotics isolated from a strain of Streptomyces verticillus and is freely soluble in water. It is available as a lyophilized powder for intramuscular, intravenous or subcutaneous injection. Each vial contains sterile Bleomycin sulfate equivalent to 15 units or 30 units of Bleomycin. Sulfuric acid or sodium hydroxide may be used, if necessary to adjust the pH.

Bleomycins are a group of related basic glycopeptides which differ in the terminal amine substituent of the common structural unit, Bleomycin acid. The main components of Bleomycin for Injection are Bleomycins A2 and B2. Chemically, Bleomycin A2 is N1-[3-(dimethylsulfonio)propyl]-Bleomycinamide and Bleomycin B2 is N1-[4-(aminoiminomethyl)amino]butyl]-Bleomycinamide.

Bleomycin is cytotoxic and possibly carcinogenic. Bleomycin is toxic to the lungs by any means of exposure and causes fibrosis in 10% of the patients who are treated with it. It accumulates in lung, kidney, and skin tissue. It is excreted as bleomycin (intact) by the kidneys and has a half life in blood of 1-5 hour, depending on the route of exposure and the level of kidney function of the patient. Patients with impaired kidney function excrete bleomycin more slowly. Kidney impairment from bleomycin therapy is rare and has been described as “unpredictable”.

Bleomycin has been shown cause harm to the fetuses of pregnant test animals. Exposure should be avoided during breastfeeding.

Exposure to Bleomycin may cause allergic reactions of the eyes or skin. Anaphylaxis has occurred in 1% of lymphoma patients treated with bleomycin.

Signs and Symptoms of bleomycin exposure include irritation, redness, stinging, or watering of the eyes; Redness, stinging, burning, itching of the skin. Inhalation can lead to pneumonitis and pulmonary fibrosis.
General Safe Handling and Storage Procedures

1. Review bleomycin Material Safety Data Sheet (MSDS) prior to handling the material (http://www.ehs.gatech.edu/chemical/chematix.php) or located inside the PRL Procedure Room.

2. Nitrile gloves shall be worn. Thicker, longer nitrile gloves that cover the lab coat cuffs are recommended.

3. A lab coat shall be worn whenever handling bleomycin.

4. Whenever possible, bleomycin should be purchased in sealed rubber capped vials so that it can be solubilized by injecting water into the vial cap without having to open the vial.
   - If bleomycin cannot be purchased as described above, weigh out on a draft-protected balance (clean around balance after use, whether or not you think you’ve spilled anything).

5. When working with high concentrations (i.e. stocks or powder) or for a prolonged period of time, double gloving can further reduce the risk of exposure, especially if the outer glove is replaced whenever significantly contaminated.

6. All use of bleomycin, particularly aerosol-producing procedures, should be conducted in a fume hood/biological safety cabinet. If this is not possible, contact EHS at 404-894-4635 for procedures on how to obtain and be cleared for respiratory protection. Dust/surgical masks do not provide chemical protection.

7. Areas where bleomycin is prepared and/or administered must be cleaned and decontaminated with soap and water immediately following each task. Potentially contaminated areas include bench tops, biological safety cabinet interiors, equipment, personal protective equipment, intravenous bags and tubing.

8. Always wash hands thoroughly after handling bleomycin, even when gloves are used.

9. Store away from incompatibles which include oxidizing agents, strong acids, and strong bases. Protect from heat.

10. It is recommended that personnel with preexisting dermatitis, cardiovascular impairment, or women who are pregnant consult a physician prior to working with bleomycin.

Safe Handling Procedures for those Administering Bleomycin
1. It is recommended that animals be anesthetized prior to the administration of bleomycin.

2. Persons administering bleomycin should wear long sleeved surgical gowns over their clothes or scrubs.

3. Persons administering bleomycin must be careful to avoid needle sticks from syringes and other sharps used in administration. Needles should be discarded in specifically designated sharps containers without recapping.

4. Do not administer bleomycin solutions that are discolored or contain particulate matter.

4. The entire procedure area must be cleaned using soap and water after the animals are returned to their cages.

5. Wash hands thoroughly after administering bleomycin.

**Safe Handling Procedures for Those Handling Animals/Bedding of Animals Injected with Bleomycin**

**Right-To-Know Training** which includes specific information about bleomycin is required prior to working with bleomycin-dosed rats.

PPE required for PRL staff and others working with bleomycin (bleo) exposed animals, carcasses, animal bedding, or spill clean-up.

- Safety glasses (goggles recommend)
- Long-sleeve lab coat or gown (change immediately after handling bleo-dosed animals).
- Double nitrile gloves (no latex or vinyl)

1. All bleo-dosed animals will be housed in standard cage bedding.

2. All bedding of animals injected with bleomycin will be disposed of as bio-hazardous waste.

3. Bleo-dosed animals should only be handled in Animal Transfer Stations (ATS) or surgery only, NOT in Housing Room.

4. Cages should be changed in ATS only.
   - Cages should be dumped only at dump station.

5. The PRL Sharps Use Procedure is posted and strictly followed:
• A sharp is any discarded material that may cause punctures or cuts and has been exposed to infectious or potentially infectious agents. This includes, but is not limited to, needles, IV tubing, and syringes with needles attached, and scalpel blades.

• Contaminated sharps must be placed in puncture proof and leak proof containers which are closed and transported to the autoclave for sterilization prior to disposal.

• Sharps should never be resheathed prior to disposal unless the sharp comes equipped with a safety device designed to be engaged after usage.

• Use sharps with safety devices whenever possible or use needleless systems to conduct research.

• Sharps should be disposed of as biohazardous waste. The outer box must be labeled to indicate that the box contains sharps to allow for proper disposal.

6. For each procedure, a small sharps container will be used that is labeled “bleomycin.”

• The sharps container will be disposed of immediately following the procedure according to Disposal Procedures.

7. A red biohazard trash can lined with red biohazard bags is located inside the PRL Procedure Room.

8. The entire procedure area must be cleaned with soap and water after the animals are returned to their cages.

9. Wash hands thoroughly after handling bleomycin.

Spills/Disposal Procedures
A minor spill is one where the individual responsible for the spill feels they are capable of handling the spill safely without the use of respiratory protection or the assistance of specially trained emergency response personnel. (Please note that our normal cut off for a minor spill is 1-4 L of material) This may include spills less than 10 mL and generating little aerosol. A major spill is any spill that requires emergency response personnel and/or requires a respirator to avoid inhalation of bleomycin. This includes spills more than 10 mL or with considerable aerosol. Clean up spills using soap and water only!

1. Individuals should become familiar with proper clean up procedures before a spill occurs (Spill kits with instructions, absorbents, and protective equipment are located inside PRL Procedure Room in case of emergency).

• For minor spills:
• Control the area of the spill by restricting access.
• For liquid spills: Clean the contaminated surface from outside to inside to avoid spreading the spill.
• For powders: Place wet paper towels over the spilled material to avoid aerosolizing material. Clean spill from outside to inside to prevent spread of contaminated area.
• Bag cleanup materials in a Biohazard bag and handle as hazardous waste (See Disposal Procedures).
• Call GT EHS at 404-894-6224 for hazardous waste pick up
• Replenish spill clean up supplies.

• For major spills:
  • Call GT Police (404-894-2500) for help (If possible, provide your name, phone number, location, and amount of material spilled)
  • Control the area of the spill by restricting access
  • For fume hood spills, close the hood sash
  • Evacuate the lab
  • Post warning signs
  • Pull fire alarm if necessary
  • Remain on site to speak to first responders

2. Clean up spills using soap and water only!

3. Any residue, contaminated soil, water, and other debris resulting from the clean up of a bleomycin spill are considered hazardous waste and must be bagged and/or boxed and disposed of in labeled biohazard containers.

Disposal Procedures
All exposed carcasses or tissues, animal bedding, spill clean-up materials, sharps containers containing bleomycin, syringes, needles, and/or activated or inactivated solutions are considered infectious and must be disposed of as hazardous waste.

1. No materials contaminated with bleomycin are to be placed in regular waste receptacles (this includes bedding of animals injected with bleomycin).

2. Tissue samples (cultures) can be autoclaved prior to being prepared for disposal via hazardous waste stream.
   • No waste streams containing bleomycin shall be disposed of in sinks or general refuse.

3. Absorbent materials (i.e. associated with spill clean-up) grossly contaminated shall be prepared for disposal as biohazardous waste.
4. All bleomycin waste containers must be suitable for transportation and must not be leaking.
   - Double bag waste in red biohazard bags and box.
   - Write Principal Investigator’s name on front of box.
   - Write PRL (Physiological Research Lab) on front of box.
   - Check the boxes for “Chemotherapeutic” and “Incinerate Only.”
   - Inform EHS that bleomycin is in the box.

5. Contact GT EHS at 4-6224 for hazardous waste pickup or use Chematix to submit a waste pickup request.
   - All bedding of animals injected with bleomycin will be disposed of as biohazardous waste.
   - When animal waste is scheduled to be disposed, it will be collected in a biohazard bag and stored as biological waste.
   - All personnel handling bleomycin must wear double gloves, lab coats, and safety glasses.

**Exposure/ Personnel Decontamination Procedures**

Bleomycin, in its powder form, can become airborne and may result in personal exposure and area contamination. Avoid creating dust. Do not inhale or ingest. Avoid contact with eyes, skin, and clothing.

1. If you are splashed with a chemical on any area of your body, you must rinse that area with copious amounts of tepid water for no less than 15 minutes. If you are splashed in an area of your body which cannot be put under a sink faucet and flooded immediately – you must use an emergency shower.
   - If your clothing is involved, remove it on the way to the shower:
     - Shout for help
     - Remain in the shower for 15 minutes
     - Get someone to call the GT police (404-894-2500)
       a) You must have the street address of where you are located
       b) Have your helper print 3 copies of the MSDS
     - Do not re-don contaminated clothing
   - If you are splashed in the eyes:
     - Shout for help
     - Hold your eyelids open with your fingers as you rinse your eyes for a full 15 minutes (move eyes up and down and side to side to fully remove chemical).
     - Have your helper watch a clock for you to make sure you continue to rinse your eyes for the full 15 minutes.
• ALL MEDICAL EXPOSURES TO THE EYES REQUIRE MEDICAL FOLLOW UP.
• EHS recommends you go to Grady Memorial Hospital to ensure proper care.
• MSDSs
  o Take one copy of the MSDS with you to the hospital
  o Give one copy to the ambulance crew
  o Give one copy to the GT Police or EHS

2. If inhaled or swallowed, seek medical attention immediately.

Procedure following a bite from a bleomycin injected rat or otherwise invasive incident (i.e. needle puncture) when using bleomycin

1. Put the animal back in its cage.
2. Wash the wound for 15 minutes with soap and vigorously running water directed at the wound.
3. Inform the PRL manager and the head of your lab.
4. Go to Grady Memorial Hospital with the MSDSs for evaluation of animal bite and exposure to bleomycin.

*If you have any (non emergency) questions please contact the Department of Environmental Health and Safety, Chemical Safety Unit: Deborah Wolfe-Lopez (404-385-2964), Ryanne Shadwick (404-385-9381) or Ryan Liska (404-385-9531)

References:

Bleomycin Official FDA information, side effects and uses.
http://www.drugs.com/pro/bleomycin.html

Faulding Labs, Bleomycin Package Insert

http://www.compliance.gatech.edu/forms/IACUC/Policies_Procedures.doc

NIOSH: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings. September 2004.

Rx Med Blomycin Sulfate
Tiva Sicor Bleomycin Sulfate Material Safety Data Sheet