
1. PURPOSE

This Standard Operating Procedure (SOP) describes the guidelines for the use of doxorubicin in rodents.

2. CONSIDERATIONS

Doxorubicin, also commonly referred to as adriamycin, is a compound clinically used as an antineoplastic drug. Research indicates that doxorubicin is potentially cytotoxic, embryotoxic, carcinogenic, teratogenic, and mutagenic.

Doxorubicin may cause irritation to the gastrointestinal tract, respiratory tract, skin, and eyes. Primary routes of occupational exposure to doxorubicin include: aerosol exposure, ingestion, accidental injection, and tissue/transplacental absorption. This SOP aims to ensure that the potential of exposure is reduced as much as possible and that these agents pose no risk to research staff, animal care personnel, and other personnel working in the animal facility.

To minimize the risk of exposure, the Principal Investigator and/or delegate(s) must identify all points of hazard and put in place safe work practices for all steps involving contact with the hazardous chemicals and drugs, as per procedures presented in this SOP and in consultation with the McGill Environmental Health and Safety (EHS) officer.

3. RESPONSIBILITY

Principal investigator (PI) and their research staff, animal care staff, veterinary care staff.

4. MATERIALS

- 4.1. Personal protective equipment (PPE):
 - 4.1.1. Safety glasses or goggles
 - 4.1.2. Nitrile gloves
 - 4.1.3. Disposable gown and sleeves
- 4.2. Chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC).
- 4.3. Absorbent pads
- 4.4. 1% bleach solution, prepared fresh daily
- 4.5. Compressed cotton fiber bedding pads (iso-PADS® Enrichment Bedding)
- 4.6. Disposal bags or containers

5. PROCEDURES

- 5.1. Prior Requirements:
 - 5.1.1. Use of doxorubicin must be described in the Facility Animal Care Committee (FACC) approved Animal Use Protocol (AUP). The MSDS must be attached to the AUP.
- 5.2. General precautions:
 - 5.2.1. Pregnant or breast-feeding women should not work with doxorubicin.
 - 5.2.2. The following personal protective equipment must be worn at all times when handling doxorubicin (in addition to the personal protective requirements of the animal room):
 - 5.2.2.1. 2 pairs of nitrile gloves
 - 5.2.2.2. Disposable gown
 - 5.2.2.3. Safety glasses or goggles
 - 5.2.3. PPE should be discarded as hazardous materials.
 - 5.2.4. Handling and preparation of solutions, including weighing of powder, and any procedure with the potential of producing aerosols, must be conducted in a certified chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC).

- 5.2.5. All containers of doxorubicin must be clearly labeled and adequately stored when not in use.
- 5.2.6. Doxorubicin must be transported in unbreakable containers.
- 5.2.7. Injections in rodents must be conducted in a certified chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC).
- 5.2.8. Work areas should be protected from spills by placing an absorbent pad with an impervious backing (absorbent material facing up). The absorbent pad is disposed of as a hazardous material.
- 5.2.9. Areas where doxorubicin is prepared and/or administered must be cleaned and decontaminated with 1% bleach solution immediately following each procedure.
- 5.2.10. Needles and sharps used with doxorubicin must be disposed of immediately in a sharps container. Do not bend or recap needles. Safety needles should be used whenever possible.
- 5.2.11. Thoroughly wash hands after handling or administering doxorubicin.
- 5.2.12. In the event of accidental exposure, promptly complete a McGill University Accident, Incident & Occupational Disease Report form: : <https://www.mcgill.ca/ehs/forms/forms/accident-and-incident-report>
- 5.3. Storage precautions:
 - 5.3.1. Doxorubicin is light sensitive; it should be kept in the dark.
 - 5.3.2. Keep containers tightly closed, preferably in a locked cabinet.
 - 5.3.3. Keep container in a cool, well-ventilated area away from sources of ignition. Recommended storage temperature is 2-8 °C.
 - 5.3.4. Do not administer doxorubicin solutions that are discolored or contain particulate matter.
 - 5.3.5. Dispose of empty containers through the Waste Management department.
- 5.4. Animal Handling and Husbandry:
 - 5.4.1. Research staff must inform the animal facility supervisor at least 1 week before administering doxorubicin to animals. This will ensure adequate preparation and availability of necessary equipment provided by the animal facility (e.g., disposal containers, PPE, bedding pads).
 - 5.4.2. Clearly indicate the hazard on the room door.
 - 5.4.3. All animal handling must be conducted in a certified chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC)
 - 5.4.4. House animals in individually ventilated cages or static microisolator cages with filter top lids.
 - 5.4.5. Consider using compressed cotton fiber bedding pads (iso-PADS®) instead of standard bedding. The pads are very absorbent, will minimize the creation of aerosols and are easier to dispose of.
 - 5.4.6. Make sure that animals are adequately restrained at the time of injection or consider using light anesthesia.
 - 5.4.7. Animals should be transferred to a clean cage immediately following doxorubicin administration.
 - 5.4.8. All cages housing animals that have been treated with doxorubicin must be clearly labeled with the following information:
 - 5.4.8.1. "Doxorubicin"
 - 5.4.8.1. Date of administration
 - 5.4.9. Animal cages should not be changed for a minimum of three days after the date of doxorubicin administration.
 - 5.4.10. Cage bedding is considered contaminated until at least 3 days after doxorubicin is no longer administered and must be disposed of in the following manner:
 - 5.4.10.1. Handle all cages in a certified chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC).
 - 5.4.10.2. To minimize the production of aerosols, moisten soiled cage bedding by spraying with water or 1% bleach solution.
 - 5.4.10.3. Place the dirty bedding or bedding pad in a biohazard bag inside the BSC.
 - 5.4.10.4. Rinse the cage with 1% bleach solution and paper towels inside the BSC.
 - 5.4.10.5. Place used paper towels in a biohazard bag inside the chemical fume hood or BSC.

- 5.4.10.6. Close the biohazard bag and place it in a second biohazard bag.
 - 5.4.10.7. Place the biohazard bags in a biohazard box, tape closed and send boxes to incineration (not autoclaving).
 - 5.4.10.8. Place clean autoclaved bedding or bedding pads in the cages (without sending them to the cage wash).
 - 5.4.10.9. Repeat steps 5.4.10.1 to 5.4.10.8 until 3 days after doxorubicin is no longer administered.
 - 5.4.10.10. Then wash the dirty cages by hand as in step 5.4.9.4, stack them in a biohazard bag and bring to cage wash area. Label the biohazard bag "Doxorubicin".
 - 5.4.10.11. Wearing mask, safety glasses or goggles, gown and nitrile gloves, open the bags and place the cages on the tunnel washer conveyor to be washed (no need to autoclave first).
- 5.5. Waste disposal:
- 5.5.1. All items contaminated or potentially contaminated with doxorubicin (e.g., needles, gloves, bedding, paper towels) must be discarded in a biohazard bag and/or box and incinerated.
 - 5.5.2. Dead animals must be double-bagged before disposal.
 - 5.5.3. Containers are incinerated by McGill's Waste Management department.
- 5.6. Small spills and leakage:
- 5.6.1. Use absorbent paper to pick up all liquid spill material. Seal the absorbent paper, as well as any of your clothing which may be contaminated, in an air-tight biohazard bag for eventual disposal.
 - 5.6.2. Wash any surfaces you may have contaminated with 1% bleach solution.
- 5.7. In case of accidental exposure:
- 5.7.1. Potential routes of exposures include: inhalation, eye contact, skin absorption, ingestion and unintentional injection.
 - 5.7.2. Report the incident immediately to your supervisor. A McGill University Accident, Incident & Occupational Disease Report form must be completed: : <https://www.mcgill.ca/ehs/forms/forms/accident-and-incident-report>
 - 5.7.3. Splash in eyes:
 - 5.7.3.1. Flush eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
 - 5.7.3.2. If required, transport the victim after flushing eyes to a hospital.
 - 5.7.4. Skin exposure:
 - 5.7.4.1. Immediately flush affected skin with water while removing and isolating all contaminated clothing.
 - 5.7.4.2. Gently wash all affected skin areas thoroughly with soap and water.
 - 5.7.4.3. If symptoms such as redness or irritation develop, seek medical attention.
 - 5.7.5. Inhalation:
 - 5.7.5.1. Immediately leave the contaminated area; take deep breaths of fresh air.
 - 5.7.6. Immediately call a physician or poison control center Ingestion:
 - 5.7.6.1. Do not induce vomiting.
 - 5.7.6.2. If the victim is conscious and not convulsing, rinse mouth with water and seek medical attention.
- 5.8. Preparation of 1% bleach solution:
- 5.8.1. Disinfectant solution must be prepared fresh daily as bleach degrades rapidly in water.
 - 5.8.2. Wear personal protective equipment when preparing and using disinfectant solution.
 - 5.8.3. Mix 1 part 5% chlorine bleach with 99 parts water.
 - 5.8.4. Label all storage containers.