Standard Operating Procedure for Working with Hazardous Chemicals in Animals

1. Health hazards and Precautions for Animal Use

The main routes of exposure to cytotoxic drugs are through the inhalation of drug particles or aerosols, skin absorption, inadvertent ingestion through contact with contaminated food or cigarettes, and needle stick injuries.

Exposure may occur during preparation and administration of the drugs, handling of body fluids from animals receiving cytotoxic drugs, handling and disposal of cytotoxic wastes and related trace contaminated material, and transportation of cytotoxic drugs. Some cytotoxic drugs have a direct irritant effect on the mucous membranes, eyes, and skin.

2. Designated Area

ABSL-1 facility with a fume hood or Type 2 biosafety cabinet (BSC) such as the one in room 1505.

3. Training

Hazardous chemical training and training on this SOP is required before working with chemotherapy drugs. This should include but is not limited to reviewing the SDS, training on the physical hazards of the chemicals, symptoms of exposure, appropriate work practices, and proper use of PPE.

4. Personal Protective Equipment (PPE)

A. Double nitrile gloves,
B. Chemical safety goggles
C. Strike proof disposable gown
D. Mask or Respirator (LARC has these available in room 1505)
E. Hair bonnet
F. Hands must be washed upon changing gloves and upon exiting animal room.
G. **Chemotherapy drugs should not be handled by persons who are pregnant or may be pregnant.

5. General Precautions for Animal Use

A. Research staff must inform the animal facility supervisor at least 48 hours before administering any chemotherapy drug to animals. This will ensure adequate preparation and availability of necessary equipment, such as hazardous waste bins, in the animal facility.
B. Animals should be restrained or anesthetized during injection.
C. Care should be taken to avoid generating aerosol during the preparation or injection procedure.
D. 5-FU, PLX, and TAM may be excreted by the animals within the first 48-72 hours
Therefore, the lab must change the bedding 72 hours after administration.

E. Doxorubicin may be excreted by the animals within first 96 hours post injection. Therefore, the lab must change the bedding 96 hours after administration.

6. **Environmental / Ventilation Controls**
The preparation of the chemotherapy drugs including reconstitution, weighing, and diluting should be performed in a fume hood or biological safety cabinet (class II Type B). Work should be done over absorbent pads or towels moistened with an appropriate disinfectant.

7. **Special Handling Procedures & Storage Requirements**
A. Chemotherapy drugs should be handled in containment and done over absorbent pads. The fume hood or other approved containment must be cleaned upon completion of tasks.
B. When transporting the chemotherapy drug(s), the vials should be placed in secondary, sealed, plastic, labeled, non-breakable containers.

8. **Animal handling practices**
A. Animals must be housed in filter top cages marked as Hazardous. Handling the cages (including bedding) will be done only by the researchers for the first 72 hours.
B. Use a class II Biological Safety Cabinet at all times (especially during injection or any surgical procedure), when performing work on these animals and/or when moving animals from dirty to clean cages.
C. Animals will be dosed with the chemotherapy drug(s) within a Class II Biosafety cabinet or designated chemical fume hood.
D. Injected animals are considered hazardous for a minimum of 72 hours after each administration of chemotherapy drug (with the exception of Doxorubicin – 96 hours); take precautions to avoid the creation of aerosols when changing or washing cages, or cleaning the room. A respirator is recommended for personnel that are immunocompromised or pregnant and for healthy personnel if work is done outside the ventilated cabinet.
E. Care should be taken to avoid exposure to bedding dust when handling exposed animals and their waste materials during this time.
F. Following the first 72/96 hours, any dead animals must be placed in primary plastic bags, which are then placed in biosafety bags for disposal following the normal LARC procedure.
G. All surfaces and racks that may be contaminated will be decontaminated with detergent solution followed by water ASAP.
H. The first cage change after each drug administration is to be done no sooner than 72 hours after the administration (with the exception of when Doxorubicin is administered). The bedding is considered contaminated and requires special handling.
   a. **All bedding from the first cage change post chemotherapy drug injection, should be handled using procedures that minimize the creation of dust and aerosols, and bedding should be changed in a fume hood or a specially designed animal bedding disposal cabinet.**
b. **When changing cages, use the following technique:**
   
i. Transfer the animals to clean cages.
   
ii. Insert the used cages in a biohazard bag.
   
iii. Twist the ends of full bags, and seal with tape. Label with tags marked “**Hazard (insert name of administered chemotherapy drug)**”.
   
iv. Water bottles, food hoppers, etc. must be wiped with an appropriate disinfectant before loading on a cart for transport.
   
vi. Transport the bags of cages to a HEPA filtered dumping station.

I. **NOTE:** 5-Fluorouracil and Doxorubicin are combustible when exposed to high temperatures and are reactive to strong oxidizing agents, such as bleach. **Therefore, bleach should never be used to clean the cages of animals that have been exposed to 5-FU or Doxorubicin.**
   
a. Run cages through the cage wash in the conventional manner.
   
i. **Note** - cage wash personnel should take extra precautions (additional PPE) when handling cages that may have chemotherapy drug contamination.
   
b. After this first cage change there is no need for further special precautions to be taken regarding the animals or the cages as long as the animals have not received any more chemotherapy drug doses.

J. Water bottles can be dumped as they normally would.

9. **Spill and Accident Procedures**
   
   **Incompatible materials:**
   
   A. **Strong oxidizing agents and strong bases are incompatible with the chemotherapeutics in this policy.**
   
   B. Spills must be cleaned immediately by properly protected trained personnel.
   
   C. **Minor Liquid Spills:** should be cleaned immediately by personnel wearing a gown, goggles, and two pairs of gloves (nitrile). Use absorbent towels to wipe liquid. The spill area should then be cleaned thoroughly with a detergent solution followed by clean water. Place waste in plastic bag and then in the chemical waste container.
   
   D. **Powder/Major Spills:** should be cleaned immediately by personnel wearing a gown, goggles, chemically-resistant gloves, and respirator, with a damp paper towel. For powder or major liquid spills outside of a fume hood or approved containment, personnel should be instructed to leave the LARC and the room should be restricted for at least 30 min. Contain or absorb the spill with absorbent towels. Collect and place waste in plastic bag and then in the chemical waste container. The spill area should then be cleaned thoroughly with a detergent solution followed by clean water- **prevent runoff into drains.** Place waste in a plastic bag and then in the chemical waste container. **Prevent, by all means available, spillage from entering drains.** Waste from a hazardous chemical spill will need to be collected by Safety Services.
   
   E. **Exposure:**
   
   F. In case of skin contact or injection with the chemotherapy drug(s), wash the affected area with soap and water for at least 15 minutes. Consult with Occupation Health.
G. For eye exposure, flush with water for at least 15 minutes. Consult with Occupational Health.
H. Report exposure incidents to your supervisor. Your supervisor will report the accident/injury to Safety Services.

10. Waste Disposal
   A. Dispose all waste material in a chemical waste container.
   B. Unused solutions of chemotherapy drugs, solid waste, or any empty containers that held the chemotherapy drug, will be disposed of as hazardous chemical material through Safety Services.
   C. Glassware and other non-porous materials can be decontaminated by soaking in an appropriate solvent (DMSO, OR NH4OH) for 24 hours.