Standard Operating Procedure for Working with Tamoxifen in Animals

1. Health hazards
   Tamoxifen (TAM) is a non-steroidal, cytotoxic chemical used to treat patients with estrogen receptor-positive breast cancer and is also FDA approved as a chemo preventative for those patients that are at a high risk of developing breast cancer. In addition, recent studies have found that TAM causes or increases endometrial cancer, as well as rare forms of uterine cancer. It is also indicated that TAM may cause mutations in the developing human genital tract. TAM may also have effects on lactation, cause harm to breast-fed children and cause reproductive toxicity.

   **Tamoxifen is a known human carcinogen, teratogen and mutagen. Pregnant women should not be exposed to Tamoxifen and should avoid handling the cytotoxin.**

2. Designated Area
   TAM requires specimens and cages to be handled in a designated area using BSL-2 level precautions for a minimum of 72 hours after TAM has been administered. After 72 hour period in the ABSL-2, cages may be moved to ABSL-1 facility with access to a fume hood or Type 2 BSC.

3. Training
   Hazardous chemical training and training on this SOP is required before working with TAM. 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
   E. Hair bonnet
   F. **Hands must be washed upon changing gloves and upon exiting animal room.**

5. General Precautions for Animal Use
   A. Research staff must inform the animal facility supervisor at least 48 hours before administering TAM 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. **TAM may be excreted by the animals within the first 72 hours post injection, therefore the lab must change the bedding 72 hours after administration.**
E. Rodents, humans, and non-human primates excrete the cytotoxic and its metabolites in feces. One major metabolite is 4-hydroxytamoxifen. Though it is not carcinogenic or mutagenic, it is still toxic and targets the liver. Mice excrete a much higher amount of 4-hydroxytamoxifen than other species.

6. **Environmental / Ventilation Controls**
   The preparation of TAM 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. TAM 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 TAM, 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 injected IP with TAM 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 TAM; 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 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. 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. The bedding is considered contaminated and requires special handling.
      a. **All bedding from the first cage change post-TAM 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-Tamoxifen”.

iv. Water bottles, food hoppers, etc. must be wiped with an appropriate disinfectant before loading on a cart for transport.

v. Transport the bags of cages to a HEPA filtered dumping station.

vi. Dump the bedding in the HEPA filtered dumping station using a chemical waste bin.

vii. Run cages through the cage wash in the conventional manner.

viii. Note - cage wash personnel should take extra precautions (additional PPE) when handling cages that may have TAM contamination.

c. 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 TAM.

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

J. All PPE should be discarded as hazardous material, i.e., in a biohazard bag, or if contaminated with TAM, as hazardous chemical waste through Safety Services.

9. Spill and Accident Procedures

Incompatible materials:
Strong oxidizing agents.

A. Spills must be cleaned immediately by properly, protected trained personnel.
   a. Minor Liquid Spills: should be cleaned immediately by personnel wearing a gown, goggles, two pairs of gloves (nitrile). Use absorbent pads to wipe liquid. The spill area should then be cleaned thoroughly with appropriate disinfectant, followed by detergent and clean water. Place waste in plastic bag and then in the chemical waste container.
   b. 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 laboratory and entrance should be restricted for at least 30 min. Contain or absorb spill with absorbent pad or vermiculite. Collect and place waste in plastic bag and then in the chemical waste container. The spill area should then be cleaned thoroughly with an, followed by detergent solution clean water- prevent runoff into drains. Place waste in a plastic bag and then in the chemical waste container.
   c. Chemical spill waste to be picked up by Safety Services.

B. Exposure:
   a. In case of skin contact or injection with TAM, wash the affected area with soap and water for at least 15 minutes. Consult with Occupation Health.
   b. For eye exposure, flush with water for at least 15 minutes. Consult with Occupational Health.
   c. 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 TAM solid waste, any empty containers that held TAM will be disposed of as hazardous chemical material through Safety Services.
   c. Glassware and other non-porous materials can be decontaminated by soaking in bleach solution for 24 hours.