OEHS POLICIES AND GUIDELINES

TITLE: Tamoxifen Treatment in Animals.

I. Use

Tamoxifen is a synthetic chemical which is most commonly used to treat Breast Cancer in women. Besides these cancer treatments, Tamoxifen is administered into animals as a research tool to trigger tissue-specific gene expression in many conditional expression constructs of genetically modified animals.

II. Toxicity

Tamoxifen is a known human carcinogen, teratogen, and mutagen.

III. Personal Protective Equipment (PPE)

When working with Tamoxifen in laboratories outside of animal facilities, PPE should include, at a minimum, a lab coat, double Nitrile gloves, and ANSI Z-87 compliant protective eyewear that provides chemical splash protection and appropriate lab attire (full-length pants, closed toe shoes, etc.)

Whenever the potential for aerosolization of prepared Tamoxifen solutions exists, procedures should be done in an appropriate containment device, such as a chemical fume hood. Outside of containment, an N95 respirator should be worn whenever the potential for inhalation exists. Note that the use of an N95 respirator requires medical clearance and fit testing to comply with 29 CFR 1910.134. Contact the Office of Environmental Health and Safety prior to purchasing or wearing respiratory protection.

When working with Tamoxifen within LASC spaces, PPE should be the same as when working at ABSL-2. This includes a head cover, eye protection, N-95 respirator, wrap-around gown, double Nitrile gloves, and shoe covers. All PPE is single use and should be disposed of in the designated biowaste container upon exiting LASC space. This PPE is required any time the microisolator cages are open (see section V)

IV. Research Animal Procedures

Because Tamoxifen is a carcinogen, a teratogen and a mutagen, it must be handled carefully. Pregnant women should not be exposed to or handle this chemical in any form.
To ensure the safety of research staff, solutions of Tamoxifen should be handled and prepared inside a chemical fume hood that has been approved by the Office of Environmental Health and Safety. Contact the Office of Environmental Health and Safety for more information. Following preparation of Tamoxifen, the work area should be thoroughly cleaned with soap and water. Any visible contamination or spills should be cleaned with a 10% bleach solution and then washed with soap and water. Any wipes contaminated with Tamoxifen must be disposed as hazardous waste.

It is recommended that animal bedding should be made of material to minimize dust generation, such as Corn-o-Cobs or Alpha pad liners. Cardboard, paper or other friable materials should be avoided whenever possible. Cage changes should take place in a cage change cabinet whenever possible. A plastic liner which can simply be rolled up and disposed of should be placed under the bedding when cage changes cannot take place in a cage change cabinet.

Administration of Tamoxifen into animals will be performed using ABSL-2-type PPE in a LASC chemical housing room (such as W839 on the 8th floor of the Center for Advanced Biomedical Research Building at 700 Albany Street).

1) Acute administration

Acute administration is typically conducted by injecting a specified dose of Tamoxifen via IP injection.

Used needles must be disposed of in an approved sharps container immediately after use. Used needles should not be set on the bench, sheared, bent or re-capped prior to disposal.

Whenever feasible, self-sheathing needles should be used to avoid the potential for accidental needle stick injuries.

To avoid the potential for inhalation of aerosols, the injection of Tamoxifen into smaller research animals should always be conducted in a certified Class II or III biosafety cabinet.

2) Chronic Administration

Tamoxifen may be administered to animals via IP injection over a course of a few days.

Chronic administration of Tamoxifen via IP should follow the same injection procedures as acute administration above.

3) Monitoring toxicity in animals during administration
Animals who have been administered Tamoxifen will not show any visual signs of toxicity after administration.

**V. Animal Housing during Chronic Administration**

Smaller animals being housed during the course Tamoxifen administration must be kept in filter-top microisolator cages to minimize the aerosolization of potentially contaminated bedding and excreta. Animals being administered Tamoxifen will be housed in ABSL-2 for at least 72 hours post-administration.

**VI. Disposal of Bedding and Carcass Waste**

Early studies of Tamoxifen have shown that rodents, humans, and non-human primates excrete the chemical 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.

Chemical hazard tags noting Tamoxifen and its potential hazards must be kept on the cages for 72 hours following the last administration to the animal. Therefore, researchers will change all bedding for this time period. The bedding should be disposed of as regulated medical waste and packaged for incineration after any cage changes made within 72 hours post Tamoxifen-administration. Likewise, all animal carcasses should be packaged for medical waste incineration after euthanasia.

**VII. Bedding Changes and Cage Washing**

Bedding changes and cage washing should be conducted in an approved cage wash facility that is maintained under negative pressure. While changing cages, personnel must wear appropriate PPE as described above. Cages should be changed inside a cage change station or other containment device during the 72 hour period post administration.

**VIII. Chemical Spills**

1) **Major spills of stock solutions**

Isolate area and report spill to the Office of Environmental Health and Safety (617-414-6666 on the Medical Campus, or 617-353-7233 on the CRC). Direct contact with the stock solution (usually in sesame or corn oil) should be avoided.

2) **Minor spills**
Don the appropriate personnel protective equipment, contain the spill and clean up bulk material using paper towel or absorbent pads from nearest chemical spill kit. For spills of powder, it may be helpful to lightly wet the absorbent material. Wipe the area with 10% bleach 1-2 times and then wash the area with soap and water. Dispose all wipes as hazardous waste.