



**TEMPLE UNIVERSITY - Research Administration
Institutional Biosafety Committee**

Standard Operating Procedure (SOP) - **Tamoxifen**

Principal Investigator: _____		Room & Building #: _____
Department: _____		Phone #: _____
Date: _____		
Location(s) Covered by this SOP.		
Building	Lab #	Procedure
_____	_____	<u>Fume hood area</u>
_____	_____	<u>Animal procedure</u>
_____	_____	<u>Animal Holding</u>

Note: The Occupational Safety and Health Administration (OSHA) requires a written SOP for any work with Particularly Hazardous Substance (PHS) in laboratories. This SOP must be customized for each lab using Tamoxifen and/or Tamoxifen solution. Insert a copy (either hard or electronic) into your chemical hygiene plan.

Research involving tamoxifen use (*in vitro* or animal studies) must be approved by the Institutional Biosafety Committee (IBC). In addition, any Animal Care and Use Protocol (ACUP) in which tamoxifen is proposed for use in animal studies must be approved by the Institutional Animal Care & Use Committee (IACUC).

Note: This SOP must be reviewed on an annual basis or whenever changes are made to use and/or location.

A. USE & PROCEDURE	Use this section to describe the process or circumstances of use, including the chemical name (IUPAC), common name, CAS #, concentration and quantity. Attach experimental protocol or written lab specific procedures.

B. GENERAL INFORMATION

- All tamoxifen work must be conducted in a Type II ducted Biosafety Cabinet (BSC). Alternatively, a certified operating chemical fume hood can be used if approved by the IBC.
- For any work conducted outside of a ducted BSC or fume hood, a full-face particle respirator type N100 must be used. Contact EHRS at 2-2520 to be fit tested.
- Individuals planning a family or pregnant can contact EHRS to schedule counseling.
- All workers must meet the training requirements listed in the training section of this SOP prior to using any tamoxifen.

C. POTENTIAL HAZARDS

- Tamoxifen is an off-white odorless solid crystalline powder with a melting point of 140-144° C.
- Tamoxifen has been classified as carcinogenic to human by IARC and NTP.
- LD50 Oral: 4100 mg/kg (rat)
- Tamoxifen is a toxic substance.
- Tamoxifen shows multiple acute effects:
 - Hazardous in case of skin contact (irritant).
 - Hazardous in case of eye contact (irritant).
 - Hazardous in case of ingestion.
 - Hazardous in case of inhalation.
- Tamoxifen is classified as a reproductive system toxin/female and a possible development toxin.
- Consult your Safety Data Sheet (SDS) for additional information.

D. PERSONAL PROTECTIVE EQUIPMENT (PPE)

The level of skin and eye protection should be selected based on the potential for splashing and other forms of exposure.

- Minimum potential for splash & exposure:
 - Double pair of chemical resistant gloves (Change gloves frequently and immediately replace with new gloves when gloves become contaminated).
 - Nitrile
 - Protective clothing shall be worn to prevent any possibility of skin contact with Tamoxifen.
 - Lab coats
 - Closed toed shoes
 - Long pants
 - Long sleeved clothing
 - Safety glasses, goggles or face shields shall be worn during operations in which Tamoxifen might contact the eyes (e.g., through vapors or splashes of solution).

- Safety glasses with side shields or chemical splash goggles - Must meet ANSI/OSHA specifications.
- When using or transferring large quantities or when using in systems under pressure.
 - Chemical splash goggles - Must meet ANSI/OSHA specifications.
 - Full-face particle respirator type N100 (if not working in a BSC or fume hood or if hood's sash is not in the down position).
 - Double pair of chemical resistant gloves (Immediately replace with new gloves when gloves become contaminated).
 - Nitrile
 - Chemical resistant apron/smock/lab coat
 - Protective Clothing
 - Impervious sleeves
 - Closed-toed shoes

NOTE: Personnel using respirators must be enrolled in the University's Respiratory Protection Program.

INSERT ADDITIONAL PPE AS NECESSARY:

E. ENGINEERING CONTROLS

- All operations involving tamoxifen (powder, granules, and solution) must be conducted in a certified ducted Biological Safety Cabinet or a properly operating or a certified chemical fume hood.
- If using tamoxifen powdered form outside of a fume hood or BSCs, a full-face particle respirator type N100 must be worn. In order to wear a full-face particle respirator, one must be medically cleared, fit tested and trained. Contact EHRS at 2-2520 to schedule fit testing.
- Syringes used for tamoxifen injection should be safety engineered type (self-sheathing syringes, luer-lock syringes, etc.).
- Safety Shower and Emergency eyewash should be easily accessible within the immediate work environment in areas where Tamoxifen is used.
- Laboratory rooms must be at negative pressure with respect to the corridors and external environment.
- Laboratory/Room doors must be kept closed at all times.

INSERT ADDITIONAL ENGINEERING CONTROL AS NECESSARY:

The nearest safety shower station is located at : _____

The nearest safety eyewash station is located at : _____

F. SPECIAL HANDLING PROCEDURES & STORAGE REQUIREMENTS

- Laboratory-specific written procedures are required for tamoxifen. Attach procedures to SOP.
- Keep container closed at all times. Open containers of tamoxifen should never be permitted.
- Once mixed into an aqueous solution, tamoxifen should then be transferred into a sealed bottle. This will prevent volatilization, spillage, and accidental contamination of the environment.
- Tamoxifen-containing chow (for small rodent users, see below for additional procedures) can be obtained from a commercial vendor.
- Store in a cool, dry, well-vented area away from incompatible substances.
- Use the smallest practical quantities for the experiment being performed.
- Transport tamoxifen-containing solutions or chow in secondary containment.
- All areas which use tamoxifen must have a chemo spill kit present.

Additional Standard Operating Procedures For Use in Small Rodents (Requires IACUC-approved ACUP):

- EHRS issued signage must be posted to the door of the room in which the tamoxifen administration to small rodents will be performed. The signage will remain on the door for the duration of the tamoxifen treatment.
- Tamoxifen may be administered to small rodents via daily intraperitoneal (i.p.) injection or oral gavage (at doses ranging from 5-100 mg/kg for up to one week) or feeding with tamoxifen-containing chow (40-80 mg/kg for 1-4 weeks).
- Injection or gavage of small rodents with tamoxifen-containing solution or changing tamoxifen-containing chow must be performed in either a certified Class II BSC hood or a certified operating chemical fume hood within ULAR facilities (as specified in approved ACUP).
- EHRS issued signage must be posted to the door of animal holding room where the small rodents are treated with tamoxifen for the duration of 72 hours from the last treatment of tamoxifen.
- A procedure card and a yellow chemo drug label sticker are placed on the cage along with the following information: 1) Tamoxifen Treatment, 2) PI of Lab and primary contact name and number, 3) date(s) of i.p. injection/oral gavage/chow administration and 4) Special handling until date (3 days after final injection/oral administration/chow feeding). Procedure card and yellow chemo drug sticker information should be clearly visible on each cage.

- After administration of tamoxifen-containing solution or chow, all surfaces must be decontaminated immediately (as outlined in the Decontamination Procedures section below).
- All contaminated disposable materials should be disposed of in appropriate designated hazardous chemo drug waste containers as outlined in the waste disposal section below. Yellow sharps containers for sharps and yellow bags for solid waste are available in all ULAR animal suites).
- For the duration of the 72 hours following the last i.p./oral administration of tamoxifen or replacement of tamoxifen-containing chow with normal chow, ULAR animal technicians should avoid handling all tamoxifen-marked cages until study completion and the removal of labeling.
- If necessary, before 72 hours has passed since the final tamoxifen administration, the cages must only be opened in either a certified Class II BSC hood or a certified operating chemical fume hood within ULAR facilities and all dirty bedding, unused tamoxifen-containing chow (if applicable), etc. disposed of in yellow bags as outlined in the Waste Disposal section below. All cage materials, including cages, diet trays and wire bar lids, will be cleaned in a routine fashion following a wipe-down with 70% ETOH solution.
- **Note:** Tamoxifen metabolism is hepatic, with excretion of metabolites largely restricted to the feces. Metabolite excretion continues for 2 days post-administration; therefore, care must be taken in the disposal of dirty bedding for 3 days after final administration or removal of tamoxifen-containing chow. Once the 3-day period has past from the last administration of tamoxifen, PI should move the animals to clean cages, after which no special handling of the bedding, cages or animals is required and procedure cards and door sign should be removed.

INSERT ADDITIONAL HANDLING & STORAGE REQUIREMENTS AS NECESSARY:

G. TRAINING REQUIREMENTS

- All personnel are required to complete the EHRS hazardous drugs safety training prior to working with any OSHA-defined hazardous drugs.
- The Principal Investigator (PI) must provide lab specific training to all laboratory workers specific to the hazards (physical and health) involved in working with the substance, work area decontamination and emergency procedures. In addition, the PI must review and provide a copy of the SDS and this SOP to any lab worker and animal care provider prior to working with any of the materials covered by this SOP.

- The PI must ensure that all lab personnel and animal care provider have attended the required training and/or refresher training.
- Personnel working with small rodents are required to complete IACUC mandated trainings.

H. DESIGNATED AREAS

- Designated area(s) for use and storage of tamoxifen must be established. This may be specific work benches, BSCs or chemical fume hoods.
- All chemicals must be in secondary containment with proper signage.
- (For animal areas only) EHRS issued signage is required for the container, designated work area and storage locations. Signage must follow the Safety Data Sheet (SDS) and GHS Classification 29CFR1910 (OSHA).
- Access to the designated areas shall be limited to trained and knowledgeable personnel.

INSERT LOCATION OF DESIGNATED AREA(S):

Tamoxifen storage area is located at: _____

I. SPILL PROCEDURES

- Spills-General Instructions
 - Notify others of the spill and keep spill area confined.
 - Review SDS.
 - Don appropriate PPE (double nitrile gloves, splash goggles, face shield and lab coat).
 - Extinguish all ignition sources.
 - Collect all spilled material and clean up material and place into an appropriate waste container or double lined bag yellow bag containing chemo waste markings. Label the waste container with a chemotherapeutic waste label.
 - Call EHRS at 215-707-2520 during office hour to report the spill.
 - Call Page operator at 215-707-4545 after office hour to report the spill.
- Minor Spills-Liquid
 - Neutralize and/or absorb freestanding liquid with absorbent included in a chemo spill kit, vermiculite, sand, etc. and absorbent pads.
 - Place clean up items in chemo waste container double lined with yellow plastic bag with chemo waste markings.
 - Wait 10 minutes and wash spill area with soap and water.
- Minor Spills-Solid
 - Wet paper towels or absorbent pads and gently place on top of the powder to avoid creation of dust.
 - Carefully wipe up the area and place clean up material into an appropriate waste container or double lined bag. Label the bag/container with contents.
 - Wait 10 minutes and wash spill area with soap and water.
- Major Spills-Liquid & Solid
 - Evacuate room or immediate area.
 - Call EHRS at 215-707-2520.
 - Post signs at entrances/exits notifying others of spill.
 - Provide assistance and information to spill responders.

INSERT LOCATION OF TAMOXIFEN SPILL KIT:

The spill kit is located at _____.

J. FIRST AID/ EXPOSURES

- General Instructions
 - Obtain SDS.
 - Contact Campus Police at 1-1234 if immediate medical assistance is necessary.
 - Notify Supervisor.
 - Notify EHRS at 215-707-2520 during office hour and Page operator at 215-4545 after office hour.
 - Seek medical assistance after any accidental exposure.
- Inhalation
 - Remove exposed individual to fresh air.
 - Seek medical attention.
- Skin/Body Contact
 - Remove clothing and rinse body in emergency shower for at least 15 minutes.
 - Seek medical attention.
- Eye Contact
 - Immediately rinse eyeball and inner surface of eyelid for at least 15 minutes.
 - Seek medical attention.
- Ingestion
 - Seek immediate medical attention.

INSERT LOCATION OF NEAREST STUDENT HEALTH, EMPLOYEE HEALTH AND HOSPITAL**Main Campus**

1. Employee Health Services, 1810 Liacouras Walk, fourth floor, M-F, 8:00 am - noon; 1 pm - 5:00 pm. Phone: 215-204-2679.
2. Student Health Services, 1810 Liacouras Walk, fourth floor, Mon, Tue, Thurs, Fri, 8:30 am - 5:00 pm, Wed, 10 am – 5 pm, Phone: 215-204-7500.
3. After hours: Emergency Department at Temple University Hospital, 3401 N. Broad Street, Philadelphia, PA 19140.

Health Science Center

1. Occupational Health Department at Temple Hospital, basement of Rock pavilion M-F, 8:00 am - 5:00 pm, Phone: 215-707-4455

2. Student Health Services, Student Faculty Center, Lower Basement, Room 43, M-F, 8:30 am - 4:30 pm, Phone: 215-707-4088.

3 After hours: Emergency Department at Temple University Hospital, 3401 N. Broad Street, Philadelphia, PA 19140.

K. DECONTAMINATION PROCEDURES

- All work areas, lab benches, equipment (glove boxes, hoods) and glassware where tamoxifen is prepared and/or administered should be cleaned immediately following each task completion utilizing a detergent/water solution.

INSERT ADDITIONAL DECOMTAMINATION PROCEDURES

L. WASTE DISPOSAL

- Tamoxifen solutions and powders must be disposed of only through EHRS.
- Syringes and needles used for tamoxifen injection should be disposed of in an approved yellow chemo sharps containers, Needles should never be bent, sheared, or recapped. Chemo sharps must be segregated from sharps contaminated with infectious materials.
- Use a chemo waste sticker to properly label each yellow bag or sharps container.
- Yellow chemo solid waste bags and yellow sharps containers are picked up by trained Housekeeping staff for off-site disposal.
- Any solid waste, and animal bedding collected after 72 hours of the last tamoxifen treatment must be disposed of as regulated medical waste.
- Carcasses euthanized or otherwise suspected to be contaminated with tamoxifen must be disposed of as chemotherapeutic waste up to 72 hours following the last tamoxifen treatment. The carcasses must be disposed of at the designated chemo waste freezer at ULAR facility at MERB 571 chemo animal freezer.
- Carcasses after 72 hours of the last tamoxifen treatment must be disposed of as regulated medical waste (RMW) at the designated infectious waste freezer at ULAR facility.

Note: Tamoxifen metabolism is hepatic, with excretion of metabolites largely restricted to the feces. Metabolite excretion continues for 3 days post-administration; therefore, care must be taken in the disposal of dirty bedding for 72 hours after the last administration.

INSERT ADDITONAL WASTE DISPOSAL

MERB 5th floor and PAH 6th floor ULAR animal facilities:

During the treatment of chemotherapeutic drugs the lab members will be performing the cage change as follows:

1. The tamoxifen soiled–food/bedding, procedural wastes are to be disposed of as chemotherapeutic waste during the treatment plus 72 hours.
2. The lab members don proper PPE (gloves, mask, hair cover, shoe covers, disposable gown) when performing chemo waste disposal (for example cage change).
3. The soiled cage containing food and bedding that need to be changed will be transferred to a cage change station (**cage change location:** _____). Micro-isolator is to be changed once every two weeks. Regular cage is to be changed once every week.
4. The lid of the soiled cages should be opened inside a cage change station.
5. The food and bedding should be disposed of into a yellow chemotherapeutic waste bag inside a cage changing station. ULAR operation will provide the yellow chemotherapeutic waste bag.
6. Once the yellow bag is 2/3 full, the bag should be securely sealed either by taping or tie a knot.
7. A chemotherapeutic waste sticker should be placed in each yellow bag with the information completed. EHRS or ULAR operation can provide the sticker.
8. The soiled cages will be disinfected using 10% bleach solution (label with the preparation date and expiration date). Either the ULAR operation or the PI’s lab can prepare the 10% bleach solution.
9. The yellow bag are to be placed at the Chemo Rack near the entrance of MERB 580 from the clean side of the facility, or directly in PAH 611 (soiled side entrance).
10. The disinfected soiled cages are to be placed at the Soiled Cage Rack at the hallway of MERB 580 from the clean side of the facility, or directly in PAH 611 (soiled side entrance). The soiled cages are stored at the Soiled Cage Rack for 72 hours for tunnel wash.

After the last treatment of tamoxifen plus 72 hours, all the bedding and food are to be disposed of as red bag waste (biohazard).

1. The ULAR staff will perform soiled cage change based on ULAR SOP.

M. PRINCIPAL INVESTIGATOR CERTIFICATION

I certify that I have read and understand the requirements of this Standard Operating Procedure (SOP) and that I agree to fully adhere to its requirements.

Principal Investigator Name: _____ Title: _____

Signature: _____ Date: _____

N. Date of the SOP Tamoxifen training for lab workers and animal care providers:

Name (please print)	Signature	TU ID Number	Department	Position / Title