

STANDARD OPERATING PROCEDURE

Procedure:	Working with tamoxifen
School/Department:	School of Molecular Bioscience
SOP prepared by:	Vicki Xie
Version	SMB054.2

Section 1 - Personal Protective Equipment

1. Full length lab coat/gown
2. Disposable nitrile gloves (NOT latex); double-layered
3. Proper enclosed footwear
4. Respiratory mask (N95 or PAPP or equivalent)
5. Hair tied back if long
6. Safety glasses/goggles

Section 2 – Potential Hazards + Safety Precautions

1. Prior to conducting any work with tamoxifen, designated personnel must provide training to his/her laboratory personnel specific to the hazards involved in working with this substance, work area decontamination, and emergency procedures
2. All personnel must familiarise themselves with the SDS for tamoxifen
3. Tamoxifen (CAS#10540-29-1) is a carcinogen, reproductive toxin (teratogen), and cytotoxic compound. It appears as a solid crystalline powder, is sensitive to light, has a melting point 97-98°C and is soluble in 95% ethanol at 20 mg/mL
4. Tamoxifen is a toxic substance, and hazardous in case of skin contact (irritant), eye contact, and ingestion and inhalation
5. Any sharp cutting instruments and needles for chemical administration into animals must be properly cleaned and laid out in such a way to allow easy work flow and prevent injury.
6. Workers with pre-existing medical conditions (e.g. allergy, immunocompromised state, chemical sensitivity) and workers who are pregnant or expecting pregnancy must consult with their supervisor AND medical specialist AND the university's WHS services before performing this procedure. If there are any serious concerns expressed by any of these individuals, this task must not be performed.

Section 3 – Procedure

Handling and storage

- Chemical solid or solutions must be made in chemical fume hoods and stored in clearly marked containers
- Tamoxifen liquid solutions (10 mg/mL dissolved in corn oil) can be stored at room temperature (recommended at 4°C in light-resistant container) in clearly marked secondary containers
- Signage is required for container (primary and secondary), designated work area, storage location, and animal cages stating: 'danger, carcinogen' with a purple cytotoxic symbol

Preparing tamoxifen stocks

- Ensure above PPE is donned prior to handling tamoxifen powder
- Laboratory operations is to be opened in chemical fumehood, with minimal exposure to light
- Clean surfaces with 80% ethanol (v/v) and set up all necessary equipment to allow for safe and efficient workflow
- Handle all tamoxifen solutions over plastic backed absorbent sheets (i.e. benchcoat) and disposed of appropriately when work is completed (i.e. purple cytotoxic bin)
- Tare the balance with an appropriate container for the stock solution (e.g. light-resistant glass vial)
- Prepare the minimum amount / volume to minimise chemical waste
- Dissolve tamoxifen with appropriate vehicle reagent (e.g. corn oil) and conditions
- Any laboratory equipment or surfaces that have come in contact with tamoxifen must be disposed of (cytotoxic waste) or decontaminated (wipe with soapy-water soaked paper towels) Non-porous

material (e.g. glassware) can be contaminated by soaking in bleach for 24 hours.

Animal work

- Animals administered with tamoxifen should be housed on non-dust producing bedding in the ventilated cages provided in the SMB Animal House Quarantine room. Alternatively, line the available bedding on plastic backed absorbent paper for containment
- To prevent cross-contamination of tamoxifen-laced animal waste and housing/bedding, animals are to be housed individually (i.e. vehicle and tamoxifen injected animals are separated)
- Cages of animals injected with tamoxifen must be clearly labelled with the following information: principal investigator/trained personnel, date of first injection, date of last injection, cytotoxic symbol (purple), personnel contact details, instructions quoting 'do not change cages; handle only with double-nitrile gloves, work inside a biosafety cabinet and wearing a respiratory mask'
- Ensure animals are observed for adverse side effects during and after tamoxifen administration, and adequate food and water is accessible.
- Ensure all work is done in a PC2 facility accessible to a Class II Biosafety cabinet (e.g. SMB Animal House Quarantine room)
- Clean surfaces with 80% ethanol (v/v) and set up all necessary equipment to allow for safe and efficient workflow (benchcoat, surgical instruments, liquid nitrogen/esky, etc)
- When injecting animals with tamoxifen solution, ensure appropriate doses are calculated and all animals handled as humanely as possible when performing injection
- When sacrificing animals, choose appropriate method (lethal injection, neck dislocation, decapitation – CO₂ may not be used for animals administered with tamoxifen) and ensure all animals are properly euthanised before proceeding with tissue removal
- Upon completion, soak all surgical equipment in 80%(v/v) ethanol for at least one hour before washing with soap and water and autoclaving. Dispose of any disposable sharps in sharps bins and clean work area when finished. Decontaminate everything to be taken out of the PC2 lab

Section 4 – Disposal / Spills / Incidents

Precaution must be taken while tamoxifen is being administered to animals AND for 72 hours beyond final administration

a) Disposal

Animal Bedding

- Wear appropriate PPE listed above
- Collect bedding into a biohazard bag inside a Class II Biosafety cabinet – cage changes must be handled using procedures that minimise production of aerosols to minimise exposure
- All disposable bedding changed during chemical administration and for 72 hours beyond final administration must be collected in purple bin for cytotoxic waste disposal

Animal tissues

- Ensure tissue is processed in a Class II Biosafety cabinet
- All carcasses/leftover animal tissues collected must be stored at -20 °C in the allocated freezers and disposed of by animal staff. All tissues must be disposed of as hazardous biological waste (see risk assessment and SOP for this)

Disposable lab supplies

All disposable solid waste generated (e.g. gloves, tissues, containers, packaging) that have been in contact with tamoxifen-administered animals are to be collected in biohazard bags for disposal into cytotoxic bin. Biohazard bags must be closed and marked with "tamoxifen containing waste".

Excess tamoxifen solids and solutions

All excess tamoxifen generated from experiments (eg. left over tamoxifen solution/powder) must be disposed of as hazardous chemical waste in the purple cytotoxic waste bin.

Sharps

All needles and syringes used to administer tamoxifen must be disposed of in separate small sharps

bins and disposed of after every experiment – labelled ‘tamoxifen-contaminated sharps’.

Cages

All cages and plastic houses are to be decontaminated by wiping with soapy water-soaked paper towels prior to standard sterilisation by animal staff.

b) Spills

- Solution: using appropriate PPE, prevent solution from spreading by applying absorbent pads, and collect into container for appropriate disposal
- Solid: if <250mg, ensure PPE is appropriate, cover material with paper towels and spray lightly with 10% (v/v) bleach and collect material and paper towels for appropriate disposal
- Source container: if container drops and breaks (1-100g), avoid raising dust, do not sweep up dry material – evacuate and restrict area, alert supervisor and SMB WHS safety officer immediately

c) Incidents

1. In case of minor skin contact/exposure: wash affected area with water
2. In case of prolonged exposure: wash affected area immediately for 15 min with soap and water; eyes flush for 15 minutes.
3. Contaminated clothing must be removed immediately and washed thoroughly.
4. In case of ingestion: DO NOT induce vomiting, give milk, activated charcoal or water and get medical attention immediately.
5. In case of inhalation: remove rapidly to clean air; administer rescue breath in if necessary and call emergency services. Seek medical attention immediately.
6. In case of needle stick/puncture exposure: wash affected area with soap and warm water for 15 min. All needle stick/puncture exposures MUST be reported to authorities.
7. Any injuries, incidents or near misses (dangerous situations not resulting in an incident) must be reported to your supervisor and via the online reporting system

Section 5 – Repairs / Certification / Validation

- All personnel working with tamoxifen must be provided with a copy of this SOP and a copy of the tamoxifen SDS, and have attended appropriate laboratory safety training (i.e. PC2, animal handling, working with hazardous chemicals training courses)
- Ensure chemical fume hood is certified (this requires an annual inspection)
- Ensure Class II Biosafety cabinet is certified (this requires an annual inspection)

Section 6 – Relevant Material safety data sheets

- Check relevant SDS for any chemicals used, especially tamoxifen (CAS#10540-29-1), anaesthetics (e.g. ketamine) and preservatives (e.g. formaldehyde)

Section 7 - References


1. Sigma Aldrich SDS for tamoxifen
2. <http://www.sigmaaldrich.com/MSDS/MSDS/PleaseWaitMSDSPage.do?language=&country=AU&brand=SIGMA&productNumber=T5648&PageToGoToURL=http://www.sigmaaldrich.com/catalog/product/sigma/t5648?lang=en®ion=AU>
3. safety.healthsciences.ucla.edu/files/view/sop/Tamoxifen.doc
4. www.dehs.umn.edu/Docs/ExampleSOP_TamoxifenInjection.doc
5. www.uthsc.edu/safety/pdfs/Tamoxifen_SOP.doc
6. SOP and risk assessment for working with animals and animal tissues (SMB002)
7. SOP and risk assessment for Class II Biosafety cabinet (SMB005)
8. SOP and risk assessment for handling toxic chemicals (SMB034)
9. SOP and risk assessment for disposing of biological wastes (SMB039)
10. SOP and risk assessment for biohazard spill (SMB004)

SOP Consultation, Training and Approval

Print names and enter signatures and dates to certify that the persons named in this section have been consulted/trained in relation to the development and implementation of this Standard Operating Procedure. WHS Representative (WHS Committee) certifies that consultation has taken place.

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Name Authorising (Printed): DIANNE FISHER.....

Signature:  **Date:** 30/3/15

WHS Committee Representative Name (Printed): MARKUS HOFER.....

Signature:  **Date:** 30/3/15