McGill

STANDARD OPERATING PROCEDURE #717

USE OF TAMOXIFEN IN RODENTS

1. PURPOSE

This Standard Operating Procedure (SOP) describes the guidelines for the use of tamoxifen in rodents.

2. CONSIDERATIONS

All chemical hazards must be listed in an approved Animal Use Protocol (AUP).

Tamoxifen is a synthetic estrogen receptor modulator which is commonly used to treat breast cancer in women. In animal research, tamoxifen is used as a research tool to trigger tissue-specific gene expression in genetically modified animals.

Tamoxifen is a known human carcinogen, teratogen, and mutagen; it must be handled carefully. It causes eye and skin irritation; may cause respiratory and digestive tract irritation if swallowed causing reproductive and fetal effect.

This SOP aims to ensure that the potential of exposure is reduced as much as possible and that these agents pose no risk to research staff, animal care personnel, and other personnel working in the animal facility.

To minimize the risk of exposure, the Principal Investigator and/or delegate(s) must identify all points of hazard and put in place safe work practices for all steps involving contact with tamoxifen, as per procedures presented in this SOP and in consultation with the McGill Environmental Health and Safety (EHS) Officer.

3. RESPONSIBILITY

Principal investigator (PI) and their research staff, animal care staff, veterinary care staff.

4. MATERIALS

4.1. Personal protective equipment (PPE):
- 4.1.1. Two pairs of nitrile gloves
- 4.1.2. Gown or lab coat
- 4.1.3. Sleeve covers
- 4.1.4. Procedure mask
- 4.1.5. Fit-tested N95 respirator (for cage processing)

4.2. Chemical fume hood, Class II Type B1 or Class II Type B2 Biological Safety Cabinet (BSC)

4.3. Absorbent pads

4.4. 70% alcohol

4.5. Compressed cotton fiber bedding pads (iso-PADS® Enrichment Bedding)

4.6. 18G, 25G, 26G needles

4.7. Luer lock syringes

4.8. Shock-resistant secondary container for transport of tamoxifen

4.9. CSA-approved sharps disposal container

4.10. Waste disposal bags and boxes

5. GENERAL PRECAUTIONS

5.1. Use of tamoxifen must be described in the Facility Animal Care Committee (FACC) approved Animal Use Protocol (AUP).

5.2. Safety Data Sheet (SDS) for the chemical hazards should be readily available, e.g., in McGill's myLab catalog, and research staff and animal facility staff should be familiar with the SDS.

5.3. Women who are pregnant, expecting to become pregnant, or nursing should not handle or be exposed to tamoxifen or feces/urine of animals treated with tamoxifen. Refer to the University Laboratory Safety Committee's (ULSC) Policy on Reproductive Health in the Laboratory.

5.4. Tamoxifen is excreted in the feces and urine of animals after administration, consequently, the procedures in this SOP must be followed when handling animals and bedding for seven days after the final tamoxifen administration.

5.5. Storage precautions and transportation:

5.5.1. All containers of tamoxifen must be clearly labeled and adequately stored when not in use. Protect from moisture, incompatible materials, and strong oxidizing agents.

5.5.2. Storage and transport containers should be unbreakable, rigid, shock-resistant, leak-proof, and made of a non-reactive material which can be easily cleaned and decontaminated in the event of a leak.

5.5.3. Tamoxifen is light sensitive and should be made and stored in a light-blocking vessel (amber, or foil wrapped). After tamoxifen is in solution, store at 4°C for the duration of injections.

5.5.4. Dispose of empty containers by incineration through the Waste Management department.

5.6. Personal protective equipment (PPE) must be worn at all times when handling tamoxifen, in addition to any PPE requirements of the animal room. Wash hands after removing PPE.

5.7. Needles and sharps used with tamoxifen must be disposed of immediately in a sharp container. Do not bend or recap needles. Safety needles should be used whenever possible.

5.8. Thoroughly wash hands after handling or administering tamoxifen.

5.9. Use a 70% alcohol solution for decontamination of equipment and areas exposed to tamoxifen. Avoid use of oxidizing agents such as accelerated hydrogen peroxide (Peroxigard, Prevail) or bleach solutions.

5.10. All cages housing animals that have been treated with Tamoxifen must be clearly labeled with the following information:

5.10.1. Name of agent: tamoxifen

5.10.2. Date(s) of administration

5.10.3. Contact name

5.10.4. The recovery date or the date cages are no longer considered hazardous, i.e., 7 days after the last administration.

6. PROCEDURES

6.1. Preparation of tamoxifen solutions:

6.1.1. Any handling, including weighing of powder, preparation of dilutions, filling syringes, and any procedure with the potential of producing aerosols, must be conducted in a certified chemical fume hood or in a Class II **Type B2** BSC.

6.1.2. Work areas should be protected from spills by placing an absorbent pad with an impervious backing (absorbent material facing up).

6.1.3. Areas where tamoxifen is prepared or handled must be cleaned and decontaminated immediately following each procedure using a 70% alcohol solution.

6.2. Tamoxifen administration:

6.2.1. Tamoxifen could be administered by several routes, including intraperitoneal injection, by oral gavage, or in food.

6.2.2. For injection/gavage dissolve tamoxifen in pharmaceutical grade corn oil to a final concentration of 10-20 mg/ml.

6.2.3. Intraperitoneal injection:

6.2.3.1. Limit injection volume to 10 ml/kg.

6.2.3.2. Repeated intraperitoneal administration of corn oil may trigger peritoneal inflammation.

6.2.3.3. Use luer lock syringes for the administration as the corn oil mixture is viscous. Draw up tamoxifen using an 18G needle, administer intraperitoneally using a 26G or 25G needle.

6.2.4. Oral gavage:

6.2.4.1. Use a 1 mL syringe and a 22-gauge feeding needle.

6.2.4.2. Limit the volume to 5 mL/kg.

6.2.5. Diets with tamoxifen are available from commercial sources.

6.3. Animal Handling and Husbandry:

6.3.1. House rodents in microisolator cages with filter top lids.

6.3.2. Consider using compressed cotton fiber bedding pads (iso-PADS®) instead of standard bedding to minimize the creation of aerosols.

6.3.3. All animal handling, tamoxifen administration, and cage manipulations must be conducted in a chemical fume hood, Type II B1 BSC, or Type II B2 BSC for at least 7 days after the final administration.

6.3.4. When using a Type II B1 BSC, note that only pre-filled syringes must be used, i.e., syringes filled in a chemical fume hood or Type II B2 BSC.

6.3.5. Work areas should be protected from spills by placing an absorbent pad with an impervious backing (absorbent material facing up).

6.3.6. Clean and decontaminate area after handling or administration using a 70% alcohol solution. The absorbent pad is disposed of as a hazardous material.

6.3.7. Cage bedding is considered contaminated at least 7 days after the last tamoxifen administration. Cages must be clearly labelled with all the administration date(s). During this period, change cages in the following manner:

6.3.7.1. Protect work area by placing an absorbent pad with an impervious backing, absorbent material facing up.

6.3.7.2. Place a waste bag inside the chemical fume hood or BSC.

6.3.7.3. Place a clean, empty cage with lid inside the chemical fume hood or BSC.

6.3.7.4. Bring the cages to the chemical fume hood or BSC. Transfer animals to the clean empty cage. Discard soiled bedding or bedding pad in the waste bag.

6.3.7.5. Spray the cage with 70% alcohol solution and wipe clean. Place used paper towels in the waste bag.

6.3.7.6. Place clean autoclaved bedding or bedding pads in the cleaned cages (cages are not sent to cage wash). Return animals to the cage. Replenish food and water as needed.

6.3.7.7. When finished, clean transfer cage by spraying the cage with 70% alcohol solution and wipe clean. Place a lid to cover the cage and bring to cage wash area for processing as described in section 6.3.9.

6.3.7.8. Roll absorbent pad with the absorbent material towards the inside and place in the waste bag. Discard the outer pair of gloves and close the waste bag.

6.3.7.9. Place the waste bag in the biohazard box. When box is full, tape closed, document the type of waste on the box and send to incineration (not autoclaving).

6.3.8. When cage bedding is no longer considered contaminated (7 days after the last tamoxifen administration), change cages in the following manner:

6.3.8.1. Follow steps 6.3.7.1. to 6.3.7.5 but transfer animals to a clean cage with standard bedding. Change the grill, food, water bottle or valve, and filter top lid.

6.3.8.2. Return animals to standard housing conditions. Remove any cage labels but leave name of chemical hazard and administration date(s).

6.3.8.3. Stack the empty cages and transport to the cage wash area covered with filter top lids.

6.3.9. Cage washing:

6.3.9.1. Do not autoclave used cages before processing.

6.3.9.2. Wearing the following PPE when processing soiled cages:

6.3.9.2.1. Designated lab coat or gown

6.3.9.2.2. Gloves and sleeves

6.3.9.2.3. N95 respirator

6.3.9.2.4. Face shield or goggles

6.3.9.3. Empty soiled bedding in a certified, ventilated and filtered bedding disposal unit. Wash cages as usual.

6.3.9.4. Wash cages with an automated washer.

6.4. Small spills and leakage:

6.4.1. Use absorbent paper to pick up all liquid spill material.

6.4.2. Wash any surfaces you may have contaminated with a 70% alcohol solution.

6.5. Waste disposal:

6.5.1. All items contaminated or potentially contaminated with tamoxifen (e.g., gloves, bedding, paper towels) are discarded as hazardous waste by incineration.

7. SAFETY

7.1. In case of accidental exposure:

7.1.1. Potential routes of exposures include inhalation, skin absorption, ingestion, and unintentional injection.

7.1.2. Report the incident immediately to your supervisor. A McGill University Accident, Incident & Occupational Disease Report form must be completed https://www.mcgill.ca/ehs/forms/forms/accident-and-incident-report

7.1.3. Splash in eyes:

7.1.3.1. Flush eyes with water or normal saline solution for 15 minutes. Remove contact lenses.

7.1.3.2. Seek medical attention after flushing eyes.

7.1.4. Skin exposure:

7.1.4.1. Immediately flush affected skin with water while removing and isolating all contaminated clothing.

7.1.4.2. Gently wash all affected skin areas thoroughly with soap and water. Rinse for 15 minutes

7.1.4.3. If symptoms such as redness or irritation develop, seek medical attention.

7.1.5. Inhalation:

7.1.5.1. Immediately leave the contaminated area; take deep breaths of fresh air.

7.1.5.2. Immediately call a physician or poison control center.

7.1.6. Ingestion:

7.1.6.1. Do not induce vomiting.

7.1.6.2. Give 1 or 2 glasses of water and immediately call a hospital or poison control center.

8. REFERENCES

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8.3. Hubbard JS, Chen PH, Boyd KL. Effects of Repeated Intraperitoneal Injection of Pharmaceutical-grade and Nonpharmaceutical-grade Corn Oil in Female C57BL/6J Mice. *J Am Assoc Lab Anim Sci* 2017;56:779-785.

8.4. Jahn HM, Kasakow CV, Helfer A, et al. Refined protocols of tamoxifen injection for inducible DNA recombination in mouse astroglia. *Sci Rep* 2018;8:5913.

8.5. Wayne NL, Duarte-Vogel S, Kraemer S, et al. Exposure assessment of laboratory workers to hazardous waste from mice treated with tamoxifen and bromodeoxyuridine. *J Chem Health Saf* 2019;26:2-8.

8.6. Whitfield J, Littlewood T, Soucek L. Tamoxifen administration to mice. *Cold Spring Harb Protoc* 2015;2015:269-271.

8.7. https://www.jax.org/research-and-faculty/resources/cre-repository/tamoxifen (Description of tamoxifen preparation).

TAMOXIFEN

Open only Type II B1 or B2 BSC

DATES OF ADMINISTRATION		RECOVERY DATE
1.	5.	
2.	6.	CONTACT
3.	7.	
4.	8.	