

March 20

## SOP # 006 for Tamoxifen

Standard Operating Procedure for Tamoxifen in Animals	
<b>Health Hazards</b>	<p>Tamoxifen is a synthetic cytotoxic used for the treatment of both early and advanced ER+ (estrogen receptor positive) breast cancer in pre- and post-menopausal 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. <b>Tamoxifen is a known human carcinogen, teratogen, and mutagen.</b> It causes eye and skin irritation; may cause respiratory and digestive tract irritation if swallowed causing reproductive and fetal effect. It is also approved by the FDA for the prevention of breast cancer in women at high risk of developing the disease. However, Tamoxifen is associated with an increased risk of endometrial carcinoma, and an increase of rare forms of uterine cancer (in women taking tamoxifen for the treatment or prevention of breast cancer). Research has indicated that tamoxifen may induce mutations in the developing (fetal through adolescent) human genital tract, consistent with its partial estrogen agonist activity.</p> <p><b>*Pregnant women should not be exposed to or handle this cytotoxic in any form.</b></p>
<b>Physical &amp; Chemical Properties</b>	<p>Tamoxifen is a solid crystalline powder, sensitive to light, and has a melting point 97-98°C. The chemical, physical, and toxicological properties have not been thoroughly investigated.</p> <p>* Its metabolites are primarily excreted in the in feces</p>
<b>Designated Area</b>	<b>ABSL2 Facility (Animal Biosafety Level 2)</b>
<b>Training Requirements</b>	<p>Hazardous chemical training and training on this SOP is required before working with Tamoxifen. 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</p>
<b>Personal Protective Equipment (PPE)</b>	<p>Double nitrile gloves or compatible chemical-resistant gloves, Chemical safety goggles, Lab coat and mask.</p> <p>Appropriate PPE should also be used for lower arms such as sleeve covers or securing gloves over the sleeves of laboratory coat.</p> <p>There are no established safe levels of exposure to cytotoxic drugs. Medical opinion is that even small quantities of cytotoxic drugs and their metabolites should be avoided as much as possible. The safest approach therefore is to reduce occupational exposure to levels as low as reasonably achievable</p>
<b>General Precautions for Animal Use</b>	<p>Tools should be adapted for BSL-2 (use safety syringe, blades and needles where possible). Have a sharps container in close vicinity.</p> <p>Animals should be restrained or anesthetized during injection.</p> <p>Exposure may occur during preparation and administration of the drugs, handling of body fluids from animals receiving cytotoxic drugs, handling and</p>



	<p>disposal of cytotoxic wastes and related trace contaminated material, and transportation of cytotoxic drugs. Some cytotoxic drugs have a direct irritant effect on the mucous membranes, eyes and skin. Spills onto skin surfaces that have cuts or abrasions and punctures of the skin with a contaminated needle or broken glass can lead to severe soft tissue injury. They should be treated immediately and observed for potential problems. Tamoxifen may be excreted by the animals within the first 72 hours post injection therefore the lab must change the bedding 72 hours after administration. 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</p>
<b>Environmental / Ventilation Controls</b>	<p>A. The preparation of Tamoxifen including reconstitution, weighing, and diluting should be performed in a <b>chemical fume hood</b>. Work should be done over absorbent pads.</p> <p>B. Work with animals should be conducted in <b>ABSL-2 facility</b>, over absorbent pads in a Class II type A2 BSC.</p>
<b>Special Handling Procedures &amp; Storage Requirements</b>	<p>A. Handling: Tamoxifen should be handled in containment and done over absorbent pads. Any visible contamination or spills should be cleaned with a 1% bleach solution and then washed with soap and water. Any wipes contaminated with Tamoxifen must be disposed as Cytotoxic hazardous waste. Utilize safe sharps procedures (i.e. sharps container in the immediate vicinity, Leurlock syringes are recommended). The fume hood or other approved containment must be cleaned upon completion of tasks. Any laboratory equipment or surfaces that have come in contact with tamoxifen must be disposed of (cytotoxic waste) or decontaminated (wipe with 0.5% bleach follow by soapy-water soaked paper towels) Non-porous material (e.g. glassware) can be contaminated by soaking in bleach for 24 hours. Upon completion, soak all surgical equipment in 80%(v/v) ethanol for at least one hour before washing with soap and water and autoclaving. When transporting Tamoxifen, the vials should be placed in secondary, sealed, plastic, labeled, non-breakable containers.</p> <p>B. All equipment must be decontaminated prior to removal from the room housing the infected animals.</p>
<b>Precautions for Animal Use</b>	<p>A. Animals should be restrained or anesthetized during injection.</p> <p>B. NO recapping needles.</p> <p>C. Have a sharps container in close vicinity.</p> <p>D. Once Tamoxifen is injected, animals, animal waste and cages are considered hazardous for a minimum 72 hours.</p> <p>E. Hands must be washed upon exiting animal room</p>
<b>Animal Handling Practices</b>	<p>A. Animals must be housed in filter top cages marked as biohazards (including the name of the chemical hazard, Tamoxifen), in negative pressurized IVC.</p> <p>B. Handling the cages (including bedding) will be done only by the researchers at least for 3day after the last administration and first cage change.</p>

	<p>C. Use a class II A2 BSC 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.</p> <p>D. Injection animals with Tamoxifen:</p> <ol style="list-style-type: none"> <li>1. Injection of Tamoxifen will be conducted within Class II A2 BSC.</li> <li>2. All needles will be disposed of in sharps container - do not recap or bend needles.</li> <li>3. Injected animals considered hazardous for a minimum of 72 hours after each administration of Tamoxifen.</li> <li>4. Take precautions to avoid the creation of aerosols when changing or washing cages, or cleaning the room</li> <li>5. Care should be taken to avoid exposure to bedding dust when handling exposed animals and their waste materials during this time.</li> <li>6. Dead animals must be placed in primary plastic bags, and then will be transferred to incineration.</li> <li>7. All surfaces and racks that may be contaminated will be decontaminated with detergent solution followed by water ASAP.</li> <li>8. 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.</li> </ol> <p>E. When changing cages use the following technique:</p> <ol style="list-style-type: none"> <li>1. Transfer the animals to clean cages</li> <li>2. Insert the used cages in a plastic bag.</li> <li>3. Twist the ends of full bags, and seal with tape. Label with wide tape or other type of label marked "Hazardous Chemical - Tamoxifen ".</li> <li>4. Transport the bags of cages to a HEPA filtered dumping station that draws air away from the user (it is recommended to use a mask or fume hood).</li> <li>5. If local ventilation controls are not available for opening cages or dumping bedding, a 3M8835 respirator and safety goggles must be worn.</li> <li>6. All contaminated bedding will be labeled as hazardous materials and handled accordingly:</li> <li>7. incinerated or placed in chemical waste bags for disposal.</li> <li>8. 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 Tamoxifen.</li> <li>9. The cages should then be put in plastic bags (marked "<b>Toxin - Tamoxifen</b>") and sealed for transport to the washroom.</li> <li>10. In the washroom, cages should be unloaded from the bags with the appropriate PPE as mentioned above and run through the cage wash in the conventional manner. Note- cage wash personnel that meet the criteria for extra precautions above (pregnant exc.) should take extra</li> </ol>
--	---



	precautions (additional PPE) when handling cages that may have Tamoxifen contamination.
<b>Spill and Accident Procedures</b>	<p>A. Spills must be cleaned immediately by properly protected trained personnel.</p> <p>B. Minor Liquid Spills: should be cleaned by personnel wearing a gown, goggles and two pairs of gloves (nitrile). Use absorbent pads to wipe liquid. The spill area should then be cleaned thoroughly with a detergent solution followed by clean water. Place waste in plastic bag and then in the chemical waste container.</p> <p>C. Powder/Major Spills: should be cleaned by personnel wearing a gown, goggles, and chemically resistant gloves. 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. In addition to the above specified PPE, a respirator and safety goggles, should also be worn. Contain or absorb spill with vermiculite. Collect and place waste in plastic bag and then in the chemical waste container. The spill area should then be cleaned thoroughly with a detergent solution followed by clean water- prevent runoff into drains. Place waste in a plastic bag and then in the chemical waste container.</p> <p>Prevent, by all means available, spillage <u>from entering drains</u>.</p> <p>D. <b><u>Exposure:</u></b></p> <ul style="list-style-type: none"> <li>• <b><i>In case of skin contact</i></b> or injection with Tamoxifen, wash the affected area with soap and water for at least 15 minutes. Consult with a Medical doctor in an Emergency Room (ER)</li> <li>• <b><i>For eye exposure</i></b>, flush with water for at least 15 minutes.</li> </ul> <p>In any case</p> <ul style="list-style-type: none"> <li>➤ <b>Consult with Medical doctor in ER</b></li> <li>➤ <b>Report incident to supervisor</b></li> <li>➤ <b>Report the accident/injury to the Safety Unit Tel: 2146/7.</b></li> </ul>
<b>Waste Disposal</b>	Dispose all waste material in the appropriate chemical waste container. Unused solutions of Tamoxifen and contaminated solid waste will be disposed of as hazardous chemical material.
I hereby confirm that I have read the SOP (Standard Operating Procedure) for Working with Tamoxifen in Animals, and agree to follow these procedures.	
<b>Name:</b> _____ <b>Title:</b> _____	