

## Tel-Aviv University –Safety Unit

### Standard Operating Procedure for Tamoxifen in Animals

<b>1. 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. It is also approved by the FDA for the prevention of breast cancer in women at high risk of developing the disease.</p> <p>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).</p> <p>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>Tamoxifen is a known human carcinogen, teratogen, and mutagen.</b></p> <p><b>*Pregnant women should not be exposed to or handle this cytotoxic in any form.*</b></p> <p>Tamoxifen is a solid crystalline powder, sensitive to light, and has a melting point 97-98°C.</p>
<b>2. Designated Area</b>	ABSL-2 facility.
<b>3. Training</b>	Hazardous cytotoxic training and training on this SOP is required before working with Tamoxifen. This should include but is not limited to reviewing the MSDS, training on the physical hazards of the cytotoxics, symptoms of exposure, appropriate work practices, and proper use of PPE.
<b>4. Personal Protective Equipment (PPE)</b>	<p>Double nitrile gloves or compatible cytotoxic-resistant gloves, Cytotoxic safety goggles, Lab coat and mask. Appropriate PPE should also be used for lower arms such as sleeve covers or securing gloves over the sleeves of laboratory coat. <b><i>Pregnant women should not be exposed to or handle this cytotoxic in any form.</i></b></p> <p><b>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.</b></p> <p><b>The safest approach therefore is to reduce occupational exposure to levels as low as reasonably achievable.</b></p>

<p>5. <b>General . Precautions for Animal Use</b></p>	<p>The main routes of exposure to cytotoxic drugs are through the inhalation of drug particles or aerosols, skin absorption, inadvertent ingestion through contact with contaminated food or cigarettes, and needle stick injuries .</p> <p>Exposure may occur during preparation and administration of the drugs, handling of body fluids from animals receiving cytotoxic drugs, handling and disposal of cytotoxic wastes and related trace contaminated material, and transportation of cytotoxic drugs.</p> <p>Some cytotoxic drugs have a direct irritant effect on the mucous membranes, eyes and skin.</p> <p>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.</p> <p>Tools (as, syringe, blades and safety needles where possible) should be adapted for BSL-2. Have a sharps container in close vicinity.</p> <p>Animals should be restrained or anesthetized during injection.</p> <p><b>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.</b></p> <p>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>
<p>6. <b>Environmental / Ventilation Controls</b></p>	<p>The preparation of Tamoxifen including reconstitution, weighing, and diluting should be performed in a fume hood or biological safety cabinet (class II Type B). Work should be done over absorbent pads.</p> <p>Following preparation of Tamoxifen, the work area should be thoroughly cleaned with soap and water.</p> <p>Work should be conducted in ABSL-2 facility, over absorbent pads in a class II type A1 or A2 biological cabinet.</p>

<p><b>5. Special Handling Procedures &amp; Storage Requirements</b></p>	<p><b>Handling:</b> 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.</p> <p>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.</p> <p>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 followed by soapy-water soaked paper towels) Non-porous material (e.g. glassware) can be decontaminated by soaking in bleach for 24 hours.</p> <p>Upon completion, soak all surgical equipment in 80%(v/v) ethanol for at least one hour before washing with soap and water and autoclaving.</p> <p>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.</b></p>
<p><b>8. Precautions for Animal Use</b></p>	<p>No recapping needles. Have a sharps container in close vicinity. Animals should be restrained or anesthetized during injection. <b>Once Tamoxifen is injected, animals, animal waste and cages are considered hazardous for a minimum of 72 hours.</b></p> <p>Hands must be washed upon exiting animal room.</p>
<p><b>7. Animal handling practices</b></p>	<p><b>1.</b> Animals must be housed in filter top cages marked as biohazards (including the name of the pathogen/biohazard). Handling the cages (including bedding) will be done only by the researchers.</p> <p><b>2.</b> Use a class II Biological Safety Cabinet 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><b>3. Injecting animals with Tamoxifen:</b> Animals will be injected IP with Tamoxifen within Class II Biosafety cabinet or designated cytotoxic fume hood.</p> <p>All needles will be disposed of in sharps container – do not recap or bend needles.</p> <p><b>4.</b> Infected animals considered hazardous for a minimum of 72 hours after each administration of Tamoxifen; take precautions to avoid the creation of aerosols when changing or washing cages, or cleaning the room.</p> <p>A respirator is recommended for personnel that are immunocompromised and for</p>

healthy personnel if work is done outside the ventilated cabinet.

5. Care should be taken to avoid exposure to bedding dust when handling exposed animals and their waste materials during this time.

6. Dead animals must be placed in primary plastic bags, which are then placed in biosafety bags for infectious waste incineration.

7. All surfaces and racks that may be contaminated will be decontaminated with detergent solution followed by water ASAP.

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.

**When changing cages, use the following technique:**

- Transfer the animals to clean cages .
- Insert the used cages in a plastic bag .
- Twist the ends of full bags, and seal with tape. Label with wide tape or other type of label marked "cytotoxic- Tamoxifen.
- Transport the bags of cages to a HEPA filtered dumping station that draws air away from the use. .(it is recommended to use a mask) or fume hood.
- If local ventilation controls are not available for opening cages or dumping bedding, an N-99 respirator and safety goggles must be worn.
- All contaminated bedding will be labeled as hazardous materials and handled accordingly :  
incinerated or placed in cytotoxic waste bags for disposal.
- 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.
- The cages should then be put in plastic bags (marked "cytotoxic- Tamoxifen") and sealed for transport to the washroom.
- 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 precautions (additional PPE) when handling cages that may have Tamoxifen contamination.

<p>9. Spill and Accident Procedures</p>	<ol style="list-style-type: none"> <li>1. Spills must be cleaned immediately by properly protected trained personnel wearing a gown, goggles, two pairs of gloves (nitrile) and respirator mask covering the mouth and nose .</li> <li>2. <b>Minor Liquid Spills:</b> should be cleaned immediately by personnel wearing a PPE. Use absorbent pads to wipe liquid. The spill area should then be cleaned thoroughly with 1% bleach (<i>allow at least 15 minutes oxidation time</i>) and then wash the area with soap and water. Place waste in plastic bag and then in the cytotoxic waste container.</li> <li>3. <b>Powder/Major Spills:</b> should be cleaned immediately by personnel wearing a PPE. 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 absorbent material, it may be helpful to lightly wet the absorbent material. Wipe the area with viusolve 1-2 times (<i>allow at least 15 minutes</i>) and then wash the area with soap and water. Collect and place waste in plastic bag and then in the cytotoxic waste container.</li> </ol> <p><b><u>Exposure:</u></b></p> <ol style="list-style-type: none"> <li>4. In case of skin contact or injection with Tamoxifen, wash the affected area with soap and water for at least 15 minutes. Consult with Employee Health Center.</li> <li>5. For eye exposure, flush with water for at least 15 minutes. Consult with Employee Health Center, Report incident to supervisor. Supervisor reports the accident/injury to the Biosafety Unit.</li> </ol>
<p>10. Waste Disposal</p>	<p>Dispose all waste material in the appropriate cytotoxic waste container. Unused solutions of Tamoxifen and contained solid waste will be disposed of as hazardous cytotoxic material.</p>
<p>I hereby confirm that I have read the SOP (Standard Operating Procedure) for Working with Tamoxifen in Animals, and agree to follow these procedures.</p>	
<p>Name:</p>	<p>Title:</p>
<p>Signature:</p>	<p>Date:</p>

