

| <b>Working with Tamoxifen and Tamoxifen-Treated Animals</b> |   |
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| <b>Uses:</b>  | Tamoxifen is a estrogen receptor modulator (SERM) drug used in the treatment or prevention of breast cancer. Other uses of Tamoxifen may include treatment of anovulatory infertility and McCune-Albright syndrome.   |
| <b>Mechanism of Action:</b>                                 | Competition with estrogen for binding sites in target tissues, induction of ovulation and blockage of specific chloride channels.   |
| <b>Adverse Health Effects:</b>                              | Adverse effects in therapeutic use are usually caused by antagonism of endogenous oestrogens, hot flushes, vaginal bleeding, irregular menses, pruritus vulvae, non-specific gastrointestinal effects (nausea and vomiting), central nervous system effects (dizziness, lethargy, depression, irritability and cerebellar dysfunction), and rare ocular effects. Adverse hematological effects have been reported, also isolated cases of death from peliosis hepatis and from hyperlipidemia. In the treatment of breast cancer, hypercalcemia and tumor flare can occur.  |
| <b>Irritant:</b>  | Unknown   |
| <b>Sensitizer:</b>  | Unknown   |
| <b>Carcinogen:</b>  | IARC Group 1: Confirmed Human Carcinogen  |
| <b>Mutagen:</b>   | Evidence of mutagenicity and genotoxicity in animals and human cell lines   |
| <b>Teratogen:</b>   | FDA Class D: There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.   |
| <b>Physical Properties:</b>                                 | White powder  |
| <b>Elimination:</b>   | Tamoxifen is mostly excreted through the biliary/fecal route (26-51%) and 9-13% is passed through the urine. Tamoxifen has an elimination half life of 24 hours and its main metabolite has an elimination half-life of 1.5days. Approximately 65% of Tamoxifen is excreted as polar conjugates (main metabolite: N-desmethyl tamoxifen) and ~30% as unchanged drug and non-polar conjugates  |
| <b>Note:</b>  | Prior to Working with TAMOXIFEN or TAMOXIFEN-Treated Animals, the Principal Investigator (PI) and Area Manager must ensure all employees who intend to work with TAMOXIFEN or TAMOXIFEN-treated animals:<br>a. Have been trained and are familiar with the contents of this procedure<br>b. If female, complete a Pregnancy - Workplace Screening Tool for Pregnant Workers form (can be downloaded from <a href="http://www.ehs.utoronto.ca">www.ehs.utoronto.ca</a> ) and submit the form to Office of Environmental Health & Safety (Fax number 416-971-1361) for evaluation and to determine if any follow-up by medical provider or accommodation is required.   |
| <b>TAMOXIFEN PREPARATION</b>                                |   |
| <b>Engineering Controls:</b>                                | TAMOXIFEN solutions must be prepared in a certified chemical fume hood. Personal protective equipment (PPE) must be worn – double gloves, goggles, and lab coat (or double gown) at a minimum. All work surfaces must be covered with absorbent, plastic-backed, disposable bench paper. If it is not possible to weigh TAMOXIFEN in a certified chemical fume hood, then:<br>- Tare an empty container with its cap;<br>- In a certified chemical fume hood, transfer an approximate quantity of TAMOXIFEN into the container;<br>- Cap and weigh the container;<br>- In a certified chemical fume hood, add an appropriate amount of solvent to achieve the desired concentration.  |
| <b>Administrative Controls:</b>                             | TAMOXIFEN and TAMOXIFEN-solutions must be stored in labeled, tightly capped containers. The container must be properly labeled with the identity of the hazardous contents (i.e. TAMOXIFEN) and the appropriate hazard warning (i.e. carcinogen). The primary container for TAMOXIFEN must be placed in a sealed, leak proof, unbreakable secondary container, which must also be labeled as described above. TAMOXIFEN as received from the manufacturer/vendor in its original undiluted or powder form must be stored separately from other chemicals in a labeled, sealed, leak proof secondary container. The storage area must be posted with an appropriate hazard label. To minimize the risk of exposure to TAMOXIFEN during reusing TAMOXIFEN and storage, TAMOXIFEN should be procured in the appropriate volume to ensure all TAMOXIFEN is used up after opening container. 8. Disposable labware should be used when preparing TAMOXIFEN solutions. TAMOXIFEN solutions must always be transported in a labeled, sealed, primary container within a sealed, leakproof, unbreakable secondary container. Adequate absorbent material must be placed within the secondary container, around the primary container, to absorb all the solution in the event of a spill. |
| <b>Personal Protective Equipment:</b>                       | Two pairs of chemical-resistant gloves (e.g. nitrile), disposable lab coat or double gown, wrist-guards or gloves taped to sleeves and mucous membrane protection (e.g. chemical goggles, face shield and surgical mask) must be worn before commencing this step.  |
| <b>Waste Disposal:</b>                                      | If non-disposable glassware is used, it must be single rinsed in a bleach solution prior to washing. The rinsate must be collected and disposed of as chemical waste. TAMOXIFEN solutions must be collected and disposed of as chemical waste. Refer to the Laboratory Hazardous Waste Management and Disposal Manual for specific instructions or contact EHS Environmental Protection Services for further information. When all work with TAMOXIFEN is complete, carefully remove all bench paper and dispose of as chemical waste. Wipe all surfaces with a bleach solution.  |
| <b>TAMOXIFEN ADMINISTRATION</b>                             |   |
| <b>Engineering Controls:</b>                                | Administration of TAMOXIFEN to rodents must be conducted in a certified chemical fume hood, certified class II type A2 biological safety cabinet at a minimum or at a certified down draft table.   |
| <b>Administrative Controls:</b>                             | Animals must be chemically or physically restrained prior to starting the procedure.<br>All work surfaces, except the down-draft table, must be covered with absorbent, plastic-backed, disposable bench paper.   |

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| <b>Personal Protective Equipment:</b>   | Both the personnel administering the TAMOXIFEN, and those in the immediate vicinity of the procedure must wear appropriate PPE. Two pairs of chemical-resistant gloves (e.g., nitrile), disposable lab coat or gown, wrist-guards or gloves taped to sleeves and mucous membrane protection (e.g., chemical goggles, face shield and surgical mask) must be worn before commencing this task.   |
| <b>Waste Disposal:</b>  | After the completion of each injection, immediately place the syringe-needle unit in a sharps disposal container.   |
| <b>Note:</b>  | Use only needle-locking syringes or disposable syringe-needle units (i.e. needle is integral to the syringe). Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated before disposal.  |
| <b>ANIMAL HOUSING</b>   |   |
| <b>For the first 3 days post-injection:</b>   |   |
| <b>Engineering Controls:</b>  | For rodents, use disposable cages if possible; cover the cages with filter bonnets<br>If cages are not filtered, they should be ventilated (i.e. via certified chemical fume hood, certified class II type A2 biological safety cabinet at a minimum or ventilated rack)  |
| <b>Administrative Controls:</b>   | The door(s) to a room containing TAMOXIFEN-treated animals must be posted in such a manner that it is clear that the room contains TAMOXIFEN-treated animals. The animal cages must also be properly labeled.<br>For large animals (Non-Human Primates and Dogs):<br>a. To minimize the creation of aerosols, line the cage drop pans with disposable, plastic-backed, absorbent pads. Adequately wet excreta with water.   |
| <b>Personal Protective Equipment:</b>   | If handling/working with TAMOXIFEN-treated animals, changing cages, disposing cages or disposing cage waste:<br>Wear disposable gown on top of gown, wrist-guards, head and foot covering, two pair chemical-resistant gloves (e.g., nitrile), N-95 disposable respirator, and chemical goggles.  |
| <b>Waste Disposal:</b>  | Carefully remove the pads and place in a hazardous waste container for disposal. If pan liners are not used, adequately wet the bedding with water to keep the dust down. Place bedding in a hazardous waste container, using care not to aerosolize dust from the bedding.   |
| <b>Note:</b>  | If entering room with TAMOXIFEN-treated animals without handling TAMOXIFEN-treated animals (cage closed):<br>Wear a standard gown, foot covering and chemical-resistant gloves (e.g. nitrile).  |
| <b>ANIMAL HOUSING</b>   |   |
| <b>3 days or more after the final TAMOXIFEN injection and before the first cage change:</b> |   |
| <b>Engineering Controls:</b>  | Cage change/dumping should be performed using certified local exhaust ventilation (e.g. certified class II type A2 biosafety cabinet at a minimum or chemical fume hood). This local exhaust ventilation should be wiped down with a bleach solution, detergent and water after use. If local exhaust is not available, the housing room is deemed contaminated for at least 2 hours after the last cage is dumped/accessed and the person dumping the cages must wear a half-face respirator (fit-tested and trained).   |
| <b>Administrative Controls:</b>   | The animals may be transferred to clean, standard caging and the TAMOXIFEN door signs and cage tags may be removed (if cages are dumped in the housing room, the room must stay marked and maintain special entry requirements for 2 hours post dumping).   |
| <b>Personal Protective Equipment:</b>   | During handling animals, changing cages and disposing cage waste:<br>Wear a disposable gown on top of gown, wrist-guards, double chemical resistant gloves (e.g., nitrile), safety glasses and mucous membrane protection (e.g. surgical mask).   |
| <b>Waste Disposal:</b>  | Disposable rodent cages must be carefully placed into hazardous waste containers, taking care to avoid creation of dusts. Contaminated bedding from reusable caging is dumped into the Red Incineration Pail within the room and the cages are wiped out with diluted bleach before removing from the room - see SOP# 3.22.3 Safe Handling of Mice Treated with Tamoxifen, for more details).<br>Dirty cages and racks should be covered with a full drape and moved to the cage wash for immediate cleaning.   |
| <b>Note:</b>  | If entering room with TAMOXIFEN-treated animals without handling TAMOXIFEN-treated animals (cage closed):<br>Lab coat or gown and foot covering must be worn before entering room.  |
| <b>EMERGENCY RESPONSE</b>   |   |
| <b>In the event of an exposure:</b>   |   |
|   | 1. Flush body area for a minimum of 15 minutes:<br>a. Contaminated skin should be washed with copious amounts of soap and water<br>b. Contaminated eyes and mucous membranes should be irrigated using normal saline or water<br>2. Notify the supervisor, if immediately available. Supervisor to fill out an incident/accident/occupational disease form and return the complete form to Health & Well-Being (Fax number: 416-971-3052).<br>3. Seek medical attention as soon as possible<br>4. If in doubt, call EHS Occupational Hygiene & Safety at 416-978-4467 to determine further steps. |
| <b>EMERGENCY RESPONSE</b>   |   |
| <b>In the event of a spill:</b>   |   |

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| <b>Small Spill</b> | <ol style="list-style-type: none"><li>1. Only employees trained in the handling of TAMOXIFEN should clean up spills</li><li>2. Wear appropriate PPE</li><li>3. If a spill occurs on linings and underpads, spray linings and underpads with a bleach solution. Allow to soak.</li><li>4. If a liquid spill occurs on an unlined surface, clean the area with plastic-backed pads to prevent TAMOXIFEN contaminating gloves. The area should be soaked with a bleach solution, rinsed with water, then washed with detergent, rinsed with water and dried with pads</li><li>5. If a solid spill occurs on an unlined surface, cover the spill with disposable towel dampened with a bleach solution</li><li>6. Discard contaminated linings, underpads and materials in hazardous waste bags</li><li>7. If in doubt, call EHS Environmental Protection Services at 416-978-7000</li></ol> |
| <b>Large Spill</b> | <ol style="list-style-type: none"><li>1. Evacuate people from the immediate area</li><li>2. During business hours, call EHS Environmental Protection Services at 416-978-7000.</li><li>3. During off-hours, contact the Campus Police.</li></ol>   |