1. PURPOSE

The intent of this Standard Operating Procedure (SOP) is to provide guidelines for the McGill University scientific community performing cancer research involving rodents.

2. RESPONSIBILITY

Facility Animal Care Committees (FACC's), principal investigator (PI) and their research staff, veterinary care staff.

3. PROCEDURES

3.1. Introduction:

3.1.1. Many questions in oncology can only be answered by in vivo studies in complex living organism. Animals with local or disseminated tumors may experience pain and/or distress, thus justifying special care and attention for their welfare. At all times, the wellbeing of the research animals should be balanced against the scientific objectives and requirements of the study. This necessitates the selection of the most appropriate clinical intervention points.

3.1.2. For the purposes of this policy cancer studies have been divided into two (2) broad categories:

3.1.2.1. Tumor biology defined as the study of how tumors grow and behave. In these types of studies, the effect of tumor burden on animals should be evaluated to avoid excessive pain or distress and to achieve research goals.

3.1.2.2. Tumor treatment is defined as the study of the response of tumors to chemical, radiologic or immunologic therapy. In these types of studies, the effect of the treatment modality on the animal should be evaluated in addition to tumor burden.

3.2. General guidelines:

3.2.1. For all in vivo cancer research, the Animal Use Protocol (AUP) must contain:

3.2.1.1. Justification of animal numbers based on a clear experimental design and a detailed statistical analysis;

3.2.1.2. Information on the expected tumor kinetic, growth characteristics and biology in the proposed model when known. The FACC reserves the right to request a pilot study if these factors are unknown.

3.2.1.3. Clearly defined experimental endpoints.

3.2.1.4. Clearly defined clinical intervention points to minimize the potential for pain and/or distress to the animal (refer to section 3.5). The selection of clinical intervention points requires detailed knowledge of the impact of the tumor biology and/or tumor treatment on the animal. The FACC may request a pilot study if these factors are unknown. Animals reaching clinical intervention points must be euthanized unless otherwise approved by the FACC.

3.3. Monitoring:

3.3.1. Monitoring is the responsibility of the PI and research staff.

3.3.2. All mice that can potentially develop tumors need to be monitored at least once weekly.

3.3.3. The frequency of monitoring should be increased during critical phases of the study, e.g., from weekly to twice a week to daily as the tumor burden increases and the humane intervention points are approaching.

3.4. Mouse models of metastasis originating from palpable tumors:

3.4.1. The cage should be identified with a distinct cage card.

3.4.2. Monitoring logs should be kept in all rooms housing tumor-bearing mice.

3.4.3. Once a tumor is palpated, a file is open for that mouse in the monitoring log book and a colored dot is place on the cage card next to the mouse identification number.

3.4.4. As the tumor burden increases, the color of the dot on the cage card is changed as follows:

3.4.4.1. Green dots: mice with a palpable tumor, with a low tumor burden, small masses < 1 cc: mice are monitored weekly but tumors are not necessarily measured.
### 3.4.4.2. Yellow dots: mice have reached approximately 50% of tumor burden endpoint. Monitoring should occur twice weekly and tumors are measured weekly.

### 3.4.4.3. Red dots: mice are approaching endpoint. Daily monitoring is necessary and tumors are measured at least twice weekly.

#### 3.5. Clinical intervention points:

<table>
<thead>
<tr>
<th>MEASURABLE OBSERVATION</th>
<th>CLINICAL INTERVENTION POINT</th>
<th>ASSESSMENT</th>
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<tbody>
<tr>
<td><strong>General Condition</strong></td>
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<tr>
<td>Hunched</td>
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<td>Rough hair coat</td>
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<td>Anorexia</td>
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<td>Cachexia</td>
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<td>Hypothermia</td>
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<tr>
<td>Abnormal behavior or vocalization</td>
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<td>Behavioral and physical examination by qualified personnel.</td>
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<td>Unresponsive to touch</td>
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<tr>
<td><strong>Tumor Clinical Properties</strong></td>
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<tr>
<td>Ulceration</td>
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<td>Scabbing, ulceration, exudates, color (deep red, purple, blue or black), heat, pain upon palpation. Animals should be individually caged and monitored for carnivorism or excessive chewing.</td>
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<td>Necrosis</td>
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<td>Infection</td>
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<tr>
<td><strong>Interference with normal functions</strong></td>
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<td>Inability to access or ingest food, to drink, to keep clean or to ambulate.</td>
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<td><strong>Local invasiveness</strong></td>
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<td><strong>Distant metastasis</strong></td>
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<td><strong>Organ specific impairment or failure</strong></td>
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<td>Behavioral and physical examination by qualified personnel. Specific organ failure assessed by physical examination and, where possible, ancillary tests (hematology, biochemistry, imagery, etc).</td>
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<tr>
<td>Respiratory: Dyspnea, tachypnea, apnea</td>
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<td>Alimentary: Chronic diarrhea, constipation, rectal prolapse, distended abdomen (ex.: ascites, ileus), jaundice</td>
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<td>Neurological: Circling, blindness, dementia, convulsion, loss of consciousness</td>
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<td>Urogenital: Anuria, polyuria, hemorrhage, discharge</td>
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<td>Myoarthroskeletal: fracture, abnormal gait or mobility</td>
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<td><strong>Body weight (BW)</strong></td>
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<tr>
<td>Adult: weight loss over 20% of initial BW</td>
<td>% = ( \frac{BW – cumulative tumor weight}{Baseline BW} ) x 100</td>
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<tr>
<td>Young: failure to maintain weight gain within 15% of age-matched control animals</td>
<td>% = ( \frac{BW}{Average, age matched, control BW} ) x 100</td>
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<tr>
<td><strong>Body condition score (BCS)</strong></td>
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<td>Physical examination by qualified personnel.</td>
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<td>Body condition score less than 2</td>
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<td><strong>Tumor Volume</strong></td>
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<tr>
<td>Mice: 2000 mm³ (2.0cc)</td>
<td>Cumulative Volume = ( \Sigma \left( \frac{3.14159}{6} \times (length \times width^2) \right) )</td>
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<td>(2.5 cc exceptionally for metastatic models)</td>
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<td>Rats: 5000 mm³ (5.0cc)</td>
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<td><strong>Tumor Burden</strong></td>
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<tr>
<td>Mice: 10% baseline BW</td>
<td>% = ( \frac{Cumulative tumor weight}{Baseline BW} ) x 100</td>
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<td>(6.0 cc exceptionally for metastatic models)</td>
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<td>Rat: over 5% baseline BW</td>
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