UBC ANIMAL CARE COMMITTEE GUIDELINES for POLICY 017

Guidelines on Monitoring and Medical Records of Animals used for Research, Teaching and Testing

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PURPOSE:

The purpose of this document is to provide details on assessing animal health in different animal models. It is intended to accompany the "Policy 017 Monitoring and Medical Records of Animal used for Research, Teaching and Testing". Minimal requirements for health assessments for rodent models are included in Appendix I. A major goal of health and welfare monitoring is to be able to quickly identify "abnormal" animals and to have a clear plan of action to address the health concerns identified.

MONITORING RECOMMENDATIONS:

1. A monitoring checklist should be developed with input from all involved with animal monitoring, including the Principal Investigator (PI) and all personnel involved with the study. Input from the clinical veterinarians, post-approval monitoring (PAM) team, and members of the ACC is encouraged. This will be particularly important for non-rodent species that may have specific monitoring requirements.

2. The clinical health variables to be recorded will vary between studies. At a minimum these should capture overall health and study specific concerns.

3. For rodents, what is included in a health assessment for monitoring should be based on recommendations listed in **Appendix IA-ID.** Additional monitoring may be required for specific studies and non-rodent species.

4. Researchers should aim to complete both invasive procedures and ACC required post-procedure monitoring within normal working hours. If surgery or other major procedures are performed late in the day or on a Friday it is expected that out of hours monitoring will be done by the study team members or specifically arranged with facility staff.

5. In many studies and for many species, especially rodent species, change in weight is a helpful measure of animal health.

6. For most surgeries, animals should be assessed for pain and analgesia for up to 3 days post-operatively (for details see "UBC Animal Care Committee Guidelines -

Rodent Procedures Classifications and Analgesia Requirements"). Analgesia must be considered appropriate if the condition is known to be painful and/or the animal shows signs of pain and there is no contraindication that would make the risk of side effects outweigh the benefit. Pain relief may be required beyond the 3rd day depending on the study. Exceptions must be approved by the committee and clearly written in the protocol.

7. The actions taken by researchers when welfare concerns are identified as a result of monitoring should follow the "Policy 004 Animal Health and Welfare Concerns: Treatment and Humane Endpoints".

Appendix IA - ID: Rodent Monitoring Sheet/Record Guidelines. Minimum expected monitoring requirements for different examples of animal models.

Appendix II: References used to create monitoring sheet/record guidelines in Appendix I.

APPENDIX IB: RODENT MONITORING SHEET/RECORD GUIDELINES - These signs should be documented for experimental monitoring Monitoring sheets and humane endpoints are approved on a per protocol basis. The frequency of monitoring MUST increase with risk of deterioration and severity of clinical signs. See Appendix 2 for References

Important: more than one column or several columns may apply to each study and additional monitoring requirements may apply

Variables	EAE	Irradiation Lethal or Sub Lethal	Sub-cutaneous Tumour studies	Internal (Orthotropic, systemic lymphoreticular) or Metastatic Tumours
Appearance Activity Posture and Gait	Every other day until clinical weakness (EAE score = 2, see "other" below) is observed/expected, then daily until EAE signs in remission for 4 days.	Daily for 14 days. Every other day if no clinical signs noted. If strain and dose (non-lethal) are already established then monitoring every third day may suffice.	Weekly until tumour palpable, then at time of tumour measurements.	Weekly until clinical signs appear or imaging, blood/serum biomarkers/palpation confirm tumour development. Daily as approaching endpoint or if tumours grow rapidly. Monitor abdominal distension for models resulting in ascites.
Body Weight initial baseline weight required	Prior to treatment, then daily once clinical weakness (EAE score = 2) is observed/expected and until EAE signs in remission for 4 days.	Daily for 14 days. Every other day if no clinical signs noted.	Once tumour is palpable and then at time of tumour measurements.	Bi-weekly to weekly body condition (typically more sensitive than weight) and weight until clinical signs appear or imaging, blood/serum biomarkers, or palpation confirm tumour development. Once tumours present, increase frequency.
Hydration	Daily once clinical weakness (EAE score = 2) is observed/expected and until EAE signs in remission for 4 days.	Daily for 14 days. Every other day if no clinical signs noted.		
Temperature				

Variables	EAE	Irradiation Lethal or Sub Lethal	Sub-cutaneous Tumour studies	Internal (Orthotropic, systemic lymphoreticular) or Metastatic Tumours
Respiration			Daily if and when risk of metastases to lung.	Daily if and when risk of metastases to lung. Breathing rate is useful.
Elimination	Check bladder and bowel function daily once clinical weakness (EAE score = 2) is observed/expected. Express bladder 2-3 times daily, if required. Monitor for penile prolapse. Continue until EAE signs in remission for 4 days.	Daily for signs of diarrhea or changes in stool consistency.		Daily production of feces and urine when abdominal/bladder tumours are present.
Neurological Signs	Every other day until clinical weakness (EAE score = 2) is observed/expected, then daily until EAE signs in remission for 4 days.		For nervous system tumour or risk of metastases to nervous system. When assessing general clinical signs monitor for: head tilt, circling, ataxia, seizures, & altered behavior.	For nervous system tumour or risk of metastases to nervous system. When assessing general clinical signs monitor for: head tilt, circling, ataxia, seizures, & altered behavior.
SKIN Incision, Wound, injection or sampling site	Daily to every other day for infection/ulceration at injection sites until ulcer heals. Daily for urine scald & penile prolapse once clinical weakness (EAE score = 2) is observed/expected and until EAE signs in remission for 4 days.	If using radiation as therapy, monitor condition of skin and local area of irradiation.	When assessing general clinical signs monitor for complications with post-injection & blood sampling sites.	When assessing general clinical signs monitor for pale extremities, indicating anemia and complications with post-injection & blood sampling sites.

Variables	EAE	Irradiation Lethal or Sub Lethal	Sub-cutaneous Tumour studies	Internal (Orthotropic, systemic lymphoreticular) or Metastatic Tumours
Tumour			Weekly tumour measurement (size, weight and volume). Note tumour weight is calculated as % of actual body weight (minus tumour). Visual assessment at time of measuring (ulceration, impairment of mobility, self-mutilation). Increase frequency as tumour approaches endpoint.	Observe and estimate size weekly by imaging, blood/serum biomarkers/palpation (if palpable). Daily as approaching endpoint or if tumours grow rapidly.
Other	Grading System for EAE Score 0 - Normal mouse, no overt signs of disease 1 - Limp tail or hind limb weakness 2- Limp tail and hind limb weakness 3- Partial hind limb paralysis 4 - Complete hind limb paralysis 5 - Moribund state, humane endpoint or death.		Note: Monitoring will depend on tumour type and body systems affected. For unfamiliar tumours, pilot studies are recommended to determine patterns of local and metastatic growth and associated adverse effects.	
Pain Assessment	Frequency of pain assessment depends on dosing interval for the drug chosen. See UBC Animal Care Committee Guidelines-Rodent Surgical Classifications and Analgesic Guidelines Animals should be monitored when the analgesia is expected to wear off (6-8h for buprenorphine, 24h for Meloxicam (Metacam) or Ketoprofen (Anafen), especially for the first 24h.			
	Pain is not expected unless scald or prolapse develops.		Daily as endpoint approaches or animal is showing signs of pain.	Daily as endpoint approaches or animal is showing signs of pain.

Variables	EAE	Irradiation Lethal or Sub Lethal	Sub-cutaneous Tumour studies	Internal (Orthotropic, systemic lymphoreticular) or Metastatic Tumours
Nursing care depends on health assessment and scientific goals of study	Once EAE score reaches a score of 2 or higher: soft bedding, long sipper tubes or gel water replacement on cage floor and /or fluid replacement (SQ fluids) and food on cage bottom. Topical treatment of injection site reactions or urine scald. Remove huts and give extra nesting if animals unable to ambulate well.	Potential for gastrointestinal and tooth damage. Give daily water supplement and soft food on cage floor. Use sterile environment +/- antibiotics.	Consider humane endpoints and affects on study data instead of extending an animal's life using nursing care. Nutritional, hydration and other support may help in some cases.	Consider humane endpoints and affects on study data instead of extending an animal's life using nursing care. Nutritional, hydration and other support may help in some cases.
Humane endpoints specific to model and referenced in the literature. Ensure typical endpoints and study-specific endpoints are included**.**	Paralysis of all 4 limbs and/or decrease in mental alertness. Inability to express bladder. Penile prolapse with swelling or ulceration of penis. Urine scald or infection of ulcerated areas, which are non-responsive to treatment. Weight loss >20% for more than 24 hours (despite rehydration).	Irradiated mice will suffer from irradiation sickness for the first 7 to 14 days. Euthanasia should be considered immediately for any mouse not recovering by day 14. All sick mice should be euthanized by 21 days, as recovery is unlikely beyond this point.	Pain that cannot be relieved by analgesia. Ascites where burden exceeds 10% of body weight (abdominal distension looks similar to a "pregnant mouse"). Tumours that interfere with locomotion or normal bodily functions. Tumour weight >10% (therapeutic) >5% (passage) of normal BW. Serious muscle atrophy or emaciation. Weight loss > 20% of BW using BW of similar normal animal. Note tumour weight is calculated as % of actual body weight (minus tumour). Ulceration or infection of the tumour site. Persistent self-induced trauma. Invasion of surrounding tissues.	

APPENDIX II: REFERENCES – Sorted in alphabetical order by model

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