UBC ANIMAL CARE COMMITTEE GUIDELINES for POLICY 017

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

Created: May 2, 2014. Revised: April 20, 2018

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 IA: 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	**Post-Surgery Minor e.g. SC implant *Class 1 or 2[1]**	**Stereotaxic Surgery *Class 2[1]**	**Post-surgery Major (Invasive) *Class 3 or 4[1]**	**Spinal Cord or Brain Injury Models *Class 4**
Appearance Activity Posture and Gait	During first 30-60min for recovery from anesthesia and 12 (Class 2) to 24 (Class 1) hours post-op, for 72 hours and then until recovered/stable.	During first 30-60min for recovery from anesthesia, then every 12 hours for at least 72 hours and then until recovered/stable.	During first 30-60min for recovery from anesthesia and 4-8h post-op, then every 8 (Class 4) to 12 (Class 3) hours daily for at least 72 hours and then until recovered/stable.	During first 30-60min for recovery from anesthesia and 4-8h post-op, then every 8 hours daily for at least 72 hours and then until recovered/stable.
Body Weight Initial baseline weight required	Daily until pre-surgery weight recovers or remains stable.	Daily until pre-surgery weight recovers or remains stable.	Daily until pre-surgery weight recovers or remains stable.	Daily until pre-surgery weight is recovered or remains stable.
Hydration	Daily until animal has recovered (at least 3 days).	Daily until animal has recovered (at least 3 days).	Daily until animal has recovered (at least 3 days).	Daily until animal has recovered (at least 3 days).
Temperature				
Respiration				
Elimination				Spinal: check bladder and bowel function 2-4x daily until bladder function returns, then weekly to detect urinary tract infections.

[1] Refer to UBC ACC Guidelines on Rodent Surgical Classifications and Analgesia

Neurological Signs		Daily until animal has recovered/stable. Monitor for: blinking, head tilt, circling, ataxia, seizures, motor deficits, & altered behavior.		1-3x daily. Monitor for: unexpected limb paresis or paralysis, autotomy, ability to access food and water, ability to urinate/defecate, seizures, unexpected ataxia, & inability to right itself.
SKIN Incision, Wound, injection or sampling site	Check incision daily for 3 days minimum. If incision inflamed, moist or opened, continue daily until healed.	Check incision daily for 3 days minimum. If incision inflamed, moist or opened, continue daily until healed.	Check incision daily for 3 days minimum. If incision inflamed, moist or opened, continue daily until healed.	Check incision daily for 3 days minimum. If incision inflamed, moist or opened, continue daily until healed. Sutures removed when incision healed (typically 10-14 days).
Tumour				
Other				
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 24 hours of a procedure.			
	Upon recovery from anesthesia, then 12-24h post-op, then daily for first 72h. Continue daily if not recovering normally.	Upon recovery from anesthesia, then 12-24 h post-op, then daily for first 72h. Continue daily if not recovering normally.	Upon recovery from anesthesia, then 4-8h post-op, then every 8-12h for first 72h. Continue daily if not recovering normally.	Upon recovery from anesthesia, then 4-8h post-op, then every 8h for first 72h. Continue daily if not recovering normally.
Nursing care depends on health assessment and scientific goals of study	Analgesia as approved in animal care protocol (minimum 24-48 hours). Additional: heat support, food on bottom of cage, fluid replacement e.g. hydrogel, & SQ fluids until recovered/stable.	Analgesia as approved in animal care protocol (minimum 48 hours). Additional: heat support, food on bottom of cage, fluid replacement e.g. hydrogel, & SQ fluids until recovered/stable.	Analgesia as approved in animal care protocol (minimum 72 hours). Additional: heat support, food on bottom of cage, fluid replacement e.g. hydrogel, & SQ fluids until recovered/stable.	Until recovered/stable: heat support, food on bottom of cage, fluid replacement e.g. hydrogel, SQ fluids.

Humane endpoints specific to model and referenced in the literature. Ensure typical endpoints and study-specific endpoints are included**.**	Dehisced or infected incision, hunched, dehydrated and/or piloerected despite nursing care. Failure to recover from anesthesia.	Dehisced or infected incision, hunched, dehydrated and/or piloerected despite nursing care. Failure to recover from anesthesia. Corneal rupture secondary to corneal damage. Seizures and other neurological signs that prevent animal from caring for itself.	Dehisced or infected incision, hunched, dehydrated and/or piloerected despite nursing care. Failure to recover from anesthesia.	Dehisced or infected incision, hunched, dehydrated and/or piloerected despite nursing care. Weight loss of >20%. Failure to recover from anesthesia. Corneal Rupture. Autonomy of >2 digits. Ruptured bladder or untreatable bladder/kidney infection. Seizures and other neurological signs that prevent animal from caring for itself.

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 IC: 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	Imaging with Anesthesia	Drug/chemical/biologic treatment with known species-specific toxic effects	Drug/chemical/biologic with unknown species-specific toxic effects. MTD studies	Diabetes Phenotype (e.g. NOD mice)	Diabetes-induced (e.g. STZ)
Appearance Activity Posture and Gait	During first 30-60 min following recovery from anesthesia, then every 12-24 hrs for 72 hrs or until recovered/stable or as long as repeated imaging continues.	Frequency dependent on severity and duration of clinical signs (range once daily to continuous). Monitor during expected phase of toxicity or side effects and until observed clinical signs resolve. If no lab specific experience with dose and/or route, monitor daily for at least 14 days after last dose.	After first administration monitor continuously over the first 30 minutes, then hourly for 2 hours and once in the following 4-8 hours. Daily monitoring required for at least the first two weeks. If clinical signs (Grade 3-4[2]) are noted then animals should be monitored twice daily. If potential for severe signs of toxicity (e.g. seizures, labored breathing, lethargy, pain) then hourly monitoring is recommended until risk decreases.	Every other day to weekly after DM onset (will depend on treatments).	Daily after administration of STZ or Alloxan.
Body Weight Initial baseline weight required	Post-imaging, daily until pre-imaging weight recovers or is stable.	Prior to treatment, daily for toxic drugs or weekly for non-toxic drugs until weight recovers or is stable. Non-toxic compounds and infrequent	Daily until weight recovers or is stable.	When blood or urine glucose or polyuria and polydipsia identified or starting at 10 weeks in NOD mice. Every other day to weekly after DM onset	Every other day to weekly after induction of DM (will depend on treatments).

Variables	Imaging with Anesthesia	Drug/chemical/biologic treatment with known species-specific toxic effects	Drug/chemical/biologic with unknown species-specific toxic effects. MTD studies	Diabetes Phenotype (e.g. NOD mice)	Diabetes-induced (e.g. STZ)
		administration by normal route does not require additional monitoring.		(will depend on treatments).	
Hydration	Daily for 72 hrs or until recovered/stable or as long as repeated imaging continues.	Drug specific as above in "appearance" category.	Minimum daily as above.	Every other day to weekly after DM onset (will depend on treatments).	Daily after injection.
Temperature					
Respiration		If potential respiratory effects then monitor at least once daily during risk period and when using oral gavage.	Minimum daily as above		
Elimination	If using radiation, monitor for diarrhea daily as above.	Drug specific: If potential gastrointesitnal effects then monitor daily during risk period.	Minimum daily as above.	Every other day to weekly after DM onset (will depend on treatments).	Daily after injection looking for indication of polyuria and polydipsia. Daily after onset of DM.
Neurological Signs		Drug specific: If potential neurological effects then monitor daily during risk period. Monitor for: head tilt, circling, ataxia, seizures, & altered behavior.	Minimum daily as above.		

Variables	Imaging with Anesthesia	Drug/chemical/biologic treatment with known species-specific toxic effects	Drug/chemical/biologic with unknown species-specific toxic effects. MTD studies	Diabetes Phenotype (e.g. NOD mice)	Diabetes-induced (e.g. STZ)
SKIN Incision, Wound, injection or sampling site	Injection Site: If injecting agents, such as contrast, monitor site of injection daily for 1-2 days. Monitor for inflammation, bleeding and infection.	IV route: if potential extravasation injury or repeated IV dosing, then check site immediately and ~ 10-45 min post injection and 1-2 d later for bruising/injury TOPICAL: if known skin irritant, monitor daily until resolved.	Minimum daily as above		
Tumour		Drug specific. If long term study of carcinogen monitor as per tumour guidelines.			
Other		If novel route and/or dose for the compound/drug follow recommendations for investigational drugs.	Potential toxicities should be well researched prior to study commencement. Pilot study required for substances with unpredictable effects.	Weekly blood or urine glucose when polyuria and polydipsia identified or starting at 10 weeks in NOD mice. Then daily to weekly after onset of DM (will depend on treatments).	Daily blood or urine glucose after administration of STZ or Allaxon. Daily to weekly after onset of DM (will depend on treatments).
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 at when the analgesia is expected to wear off (6-8h for buprenorphine, 24h for Meloxicam (Metacam) or Ketoprofen (Anafen), especially for the first 24h.				

Variables	Imaging with Anesthesia	Drug/chemical/biologic treatment with known species-specific toxic effects	Drug/chemical/biologic with unknown species-specific toxic effects. MTD studies	Diabetes Phenotype (e.g. NOD mice)	Diabetes-induced (e.g. STZ)
		Post administration & frequency appropriate for drug, if needed.	Post administration and minimum daily.		
Nursing care depends on health assessment and scientific goals of study	Heat support, food placed on bottom of cage, additional treats and gel water replacement on cage floor and /or fluid replacement (SQ fluids) until recovered/stable. Care will depend on frequency and type of imaging.	Consider humane endpoints and effects 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 effects 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 effects on study data instead of extending an animal's life using nursing care. Nutritional, hydration and other support may help in some cases. Other: Warming if hypothermic. Insulin or IP dextrose for metabolic corrections for some studies.	Consider humane endpoints and effects on study data instead of extending an animal's life using nursing care. Nutritional, hydration and other support may help in some cases. Other: Warming if hypothermic. Insulin or IP dextrose for metabolic corrections for some studies.
Humane endpoints specific to model and referenced in the literature. Ensure typical endpoints and study-specific	Typical endpoints	Typical endpoints Other: Skin necrosis at injection site or difficulty breathing post-gavage.	Typical endpoints Other: Skin necrosis at injection site or difficulty breathing post-gavage. For Toxicity or Maximum Tolerated Dose studies exceptions may be permitted.	Typical humane endpoints Other: Severe muscle weakness, inability to maintain hydration, prolonged hyperglycemia.	Typical humane endpoints Other: Severe muscle weakness, inability to maintain hydration, prolonged hyperglycemia.

Variables	Imaging with Anesthesia	Drug/chemical/biologic treatment with known species-specific toxic effects	Drug/chemical/biologic with unknown species-specific toxic effects. MTD studies	Diabetes Phenotype (e.g. NOD mice)	Diabetes-induced (e.g. STZ)
endpoints are included.					

APPENDIX ID: 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	Infectious Models Acute	Infectious Models Chronic	Colitis	Aging & Longevity	Food Restriction & Special Diets
Appearance **Activity** **Posture and Gait**	Daily or every other day, depending on course of disease.	Once or twice weekly, depending on course of disease.	1-2 times weekly until clinical signs appear, then minimum once daily.	At least monthly until onset of clinical signs of aging, then daily to weekly, depending on severity of clinical signs, if procedures performed or age exceeds normal laboratory lifespan for species.	If diet is not nutritionally complete, monitor twice weekly.
Body Weight **Initial baseline weight required**	Daily or every other day, depending on course of disease.	Once or twice weekly, depending on course of disease.	Weekly until clinical signs appear, then daily to twice weekly, depending on model severity.	At least monthly until onset of clinical signs of aging, then 1-2 times daily to weekly, depending on severity of clinical signs. Precipitous weight loss and decreased temperature have been shown to be markers of imminent death.	Once to twice weekly. Weight loss should not to exceed 20% of free feeding weight of aged matched control.
Hydration	Daily or every other day, depending on course of disease.	Once or twice weekly, depending on course of disease.	When assessing general clinical signs.	When assessing general clinical signs and particularly when approaching humane endpoint.	Twice weekly for nutritionally incomplete or special diet.

Variables	Infectious Models Acute	Infectious Models Chronic	Colitis	Aging & Longevity	Food Restriction & Special Diets
Temperature	Temperature daily or every other day, depending on course of disease. Use directed infrared scanner or implanted thermistor microchip. T is most predictive sign of impending death.	Temperature once or twice weekly, depending on course of disease. Use directed infrared scanner or implanted thermistor microchip. T is most predictive sign of impending death.Use directed infrared scanner or implanted thermistor microchip. T is most predictive sign of impending death.		As endpoint approaching measure temperature daily. Use directed infrared scanner or implanted thermistor microchip. Precipitous weight loss and decreased temperature have been shown to be markers of imminent death.	
Respiration				At least once daily as endpoint approaches or moderate respiratory signs begin.	
Elimination			Weekly until first clinical signs, then daily. Score for stool consistency, rectal bleeding and prolapse and anal irritation.	When assessing general clinical signs.	
Neurological Signs				When assessing general clinical signs. Daily if previous neurological signs present. Continue until resolution or humane endpoints reached.	

Variables	Infectious Models Acute	Infectious Models Chronic	Colitis	Aging & Longevity	Food Restriction & Special Diets
SKIN **Incision,** **Wound, injection or sampling site**				When assessing general clinical signs.	
Tumour			See internal tumour monitoring for colon cancer models e.g. azoxymethane	When assessing general clinical signs. If tumours present, consult tumour monitoring.	
Other					
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.				
Nursing care depends on health assessment and scientific goals of study	Nursing care may alter course of disease so generally not recommended. Consider negative effects of ventilated caging (i.e. hypothermia).	Nursing care may alter course of disease so generally not recommended. Consider negative effects of ventilated caging (i.e. hypothermia).	Gel water replacement on cage floor and /or fluid replacement (SQ fluids). Food on cage bottom. Other treatment generally contraindicated by study design.	Soft bedding (to minimize age-related pain), enrichment, long sipper tubes or gel water replacement on cage floor and /or fluid replacement (SQ fluids) and food on cage bottom. Analgesia or other care as per clinical signs.	Rodents will not consume water without food. Food restriction studies must not be started until rodents are at least 14 wks old, otherwise weight gain due to growth must be accounted for.

Variables	Infectious Models Acute	Infectious Models Chronic	Colitis	Aging & Longevity	Food Restriction & Special Diets
Humane endpoints specific to model and referenced in the literature. Ensure typical endpoints and study-specific endpoints are included**.**	Typical endpoints. Other: Temperature below 34.5^{o}C, severe dehydration, % daily body weight loss as predetermined in pilot studies.	Typical endpoints. Other: Temperature below 34.5C, severe dehydration, % daily body weight loss as predetermined in pilot studies.	Typical endpoints. Other: Marked rectal prolapse that is necrotic or bleeding, swollen and the animal cannot defecate	Must be clearly defined for each study and scientifically justified. Use of precipitous weight loss and decreased temperature have been shown to be markers of imminent death.	Weight loss beyond 20% or dehydration that does not respond to increased feeding.

APPENDIX II: REFERENCES – Sorted in alphabetical order by model

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