

Colorado State University
Institutional Animal Care and Use Committee
(IACUC)

Policy on Observation of Animals in Progressive Disease Studies

Progressive disease studies involve diseases that may result in the decline of the animal's health and welfare including infectious disease, tumor burden, or toxicology studies.

Experimental studies may involve procedures that cause clinical symptoms or morbidity in animals. The selection of the most appropriate endpoint(s) includes:

- Careful consideration of the scientific requirements of the study.
- The expected and possible adverse effects the research animals may experience (pain, distress, illness, etc.)
- The most likely time course and progression of those adverse effects.
- The earliest most sensitive indicators of present or impending adverse effects.

The effective use of endpoints requires that properly qualified individuals perform both general and study-specific observations of the animals at appropriate time points.

Efforts must be made to minimize pain and distress experienced by animals used in research. Optimally, studies are terminated no later than when animals begin to exhibit clinical signs of disease if this endpoint is compatible with meeting the research objectives. Such endpoints are preferable to death or moribundity as endpoints since they minimize pain and distress.

Animals on infectious disease or other studies may need to be monitored more closely for signs of distress and pain caused by inoculation with an infectious agent or other procedures. Following inoculation with an infectious agent the animals must be observed at least once within 8-12 hours. Based on the clinical scoring at that time regular observations occur as follows:

Clinical Signs/Status	Observation Frequency and/or Required Action
No clinical signs (A)	Observations will occur once daily for studies that involve infectious disease, tumor burden, or toxicology studies.
Mild clinical signs (B)	Associated with the study, observations will occur no more than 12 hours apart.
Clinical signs of moderate illness (C)	Associated with the study, observations will occur no more than 8 hours apart.
Moribund animals (D)	Animals will be euthanized.

Classification is based on the Laboratory Animal Resources (LAR) Rodent Behavioral Scoring System (Attachment 1), and can be extrapolated for other species. The definitions may be modified to reflect clinical signs associated with the species being utilized. Observation frequency is determined by the animal displaying the most significant clinical signs. For example:

- If 1 animal has moderate clinical signs (C) and the others have mild clinical signs (B), then the animals will be observed at least every 8 hours.
- If animals are not undergoing treatment of any kind, then all of the animals in the study must be observed at least every 8 hours.
- If they are undergoing treatments, then this applies only to the treatment group that demonstrated moderate clinical signs (C).

If any animal is Found Dead In Cage (FDIC) then group observations will occur every 8 hours. If not undergoing treatment of any kind, all animals on the study must be observed at least every 8 hours. If undergoing treatments, then this applies only to the treatment group in which the FDIC was found. The LAR Veterinary Staff¹ shall be contacted when an animal is FDIC, and the frequency of observations may be reduced at their discretion. If, during the course of disease, animals begin to recover and show improved signs over a 24 h period, then the frequency of observations may be reduced. For example:

- If a moderately ill animal begins to recover and the clinical signs improve over a 24 h time frame, then observations can be reduced to every 12 hours.
- If they continue to improve over the next 24 h time frame, then observations can be reduced to every 24 h. However, observation interval will still be based on the animal with the most significant clinical signs.

Observations must occur according to the specified intervals 7 days per week.

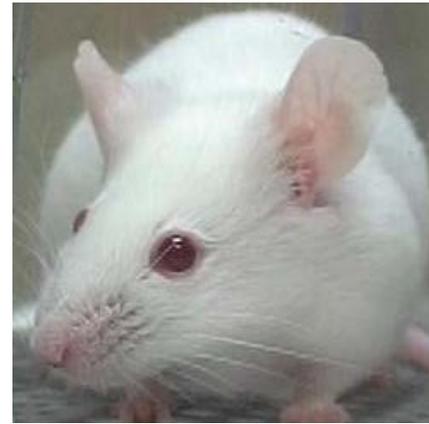
- The PIs will provide a phone tree for contact information so that individuals can contact one another as conditions change.
- All observations will be recorded in the study data and be available for review by LAR Veterinary Staff, the Post-Approval Monitor, and the IACUC. **Attachment 2** is an example Observation Record that is recommended to document these observations.

Deviations from this policy may be considered by the IACUC with adequate scientific justification

¹ LAR Veterinary Staff: includes AV/delegates, LAR Residents, LAR Veterinary Technicians

Attachment 1: LAR Rodent Behavioral Scoring System

- A. Behavior Score A represents an apparently normal animal behavior.** The animal should appear healthy and within normal behavioral limits to the trained observer. Animals should be awake when a person is in the room (except for hamsters which prefer to sleep in the daylight), well-groomed (clean, smooth coat), explore its environment or observe or build/repair nests, have a normal posture and gait (flattened back, no limping, hopping, staggering, dragging limbs or carrying them) and readily eat food and drink water. Hamsters may have to be prodded out of their sleeping nests, but after a few moments will look similar to other rodents. Note that normal behavior may be accompanied by other conditions (i.e, skin trauma, eye lesions, etc.) which need to be reported on a morbidity report.



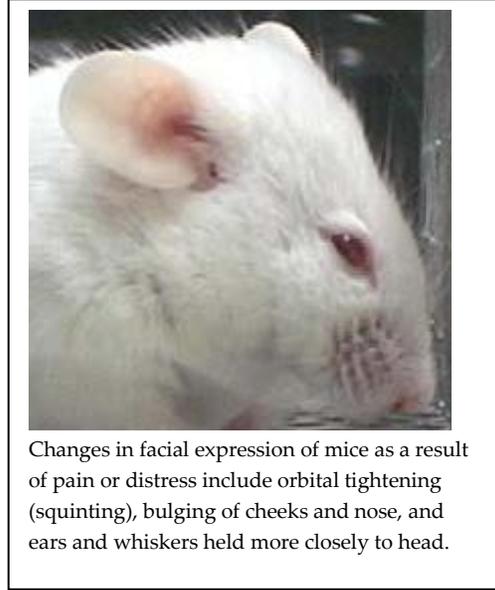
Changes in facial expression of mice as a result of pain or distress include orbital tightening (squinting), bulging of cheeks and nose, and ears and whiskers held more closely to head.

- B. Behavior Score B represents an animal with slight or subtle behavioral changes.** The animal would be noted to be slightly abnormal by the experienced and observant trained observer. It may not be grooming adequately, and the coat may look oily or rough. In rats you may see porphyrin staining on the coat, indicating stress. This animal is eating and drinking adequately but may seem a little less active than normal. It might rest in a hunched-up position, but this is transitory. This animal seems less interested than normal in his environment, other animals or people. This type of behavior may be the result of experimental manipulation or illness; if so, the animal will improve or get worse. This Behavior Score may be accompanied by gait abnormalities or other signs of trauma or illness (i.e., nasal or ocular exudate, rectal prolapse, etc.). Although only slight, this behavioral change should be reported in a morbidity report, even if it is the only abnormality seen.



Changes in facial expression of mice as a result of pain or distress include orbital tightening (squinting), bulging of cheeks and nose, and ears and whiskers held more closely to head.

C. Behavior Score C represents an animal that is definitely not acting normally, and caretakers should alert investigators and put a “watch” on the animal. This is the type of animal that an experienced observer would quickly recognize as abnormal, but not one that is significantly suffering that needs to be immediately euthanized. It is reluctant to move, and rests upright with the back hunched (*sick rodent posture*). The back typically stays rounded when the animal moves at all. The animal will move if prodded (poked with a finger or an instrument). The animal is probably not eating and drinking adequately. The animal is not grooming, and the haircoat is oily, dirty and stands up (piloerection). There are some cases in which animals may recover from this state. If animals are not euthanized at this time point, the AV veterinary staff must be consulted.



D. Behavior Score D represents a MORIBUND animal. The definition of moribund is that the animal is *near death and will not recover*. This is an animal that an experienced observer would recognize as severely compromised and suffering without the possibility of recovery. The animal is either hunched in a sick rodent posture or lying on its side. The coat is ungroomed. The only sign that it is alive is breathing, which may be shallow, slow or rapid. Eyes will be closed partially or completely and may be sunken from dehydration. The animal may be very thin, from dehydration or inappetence. If prodded or if a toe is pinched, this animal will not respond or will respond only with slight movement, not like it would if it could avoid the stimulus. The animal may feel cool to the hand if picked up (a normal animal will feel warm). This animal should have immediate euthanasia (within 2 hours). Investigators should be notified that euthanasia must be performed, or the AV staff will do it.

Institutional Endorsement

The "Policy on Observation of Animals in Progressive Disease Studies" was approved by the IACUC on 12/17/19 for recommendation to the Institutional Official supports the research, teaching and service mission of Colorado State University, and ensures that the welfare of animal subjects used therein will be protected. Therefore, as the Institutional Official, I declare the IACUC-recommended policy to be the institutional policy of the Colorado State University Animal Care and Use Program.

A handwritten signature in blue ink that reads "Alan S. Rudolph". The signature is written in a cursive style and is positioned above a solid horizontal line.

Institutional Official

19-December-2019

Date