Procedure: IACUC-64
Date: July 25, 2024
Enabled by: UCD IACUC
Supersedes: New

UC Davis
Institutional Animal Care and Use Committee (IACUC)

Title: Experimental Autoimmune Encephalitis (EAE) Mouse Model Monitoring and Care

I. Purpose:

EAE is a commonly used animal model to study Multiple Sclerosis and other demyelinating diseases. This policy is intended to provide guidance on welfare considerations that should be addressed when proposing to work with this animal model.

II. Policy:

EAE generally manifests as an ascending paralysis, and for research purposes is often graded on a 0 to 5 scale from no disease (0) to loss of tail tone (1) to moribund (5). The course may vary from one or more episodes with short periods of remission of clinical signs to a progressive chronic state. However, for animal care, the critical aspects of this model involve the ability of the animal to reach food and water and assistance with urination. The assessment, care, and recordkeeping of EAE animals are the responsibility of the Principal Investigator and their staff. These responsibilities apply 7 days per week.

All procedures related to this model must be described in the animal care and use protocol. This includes:

1. Type of induction.
2. Timeline expected for the model, disease progression, remission, relapse, and endpoint.
3. Frequency of monitoring and scoring system used.
4. Supportive care provided at disease stages.
5. Humane endpoints.
6. Potential adverse events and how they are mitigated.

III. Procedure:

A. Prior to induction an initial weight must be recorded for each animal.

B. The name of the substance(s) used to induce EAE, amount, route, and date of induction must be recorded on a hazard card placed on the cage, if applicable.

C. Animals must be observed daily and records maintained starting on the day when symptoms begin (this will vary based on the induction used). A scoring system should be used to evaluate the severity of neurologic deficits of each individual mouse daily. Clinical signs and ascending paralysis, a.k.a. neurologic condition score (NCS) is commonly assessed on a 0 to 5 point scale (see below). Other scoring systems may be used provided they are clearly defined in the animal care and use protocol and made available in close proximity to the affected animals. An example NCS Mouse Monitoring Sheet can be found in the Appendix.

D. Documentation of personel training in both diagnostic procedures, such as bladder palpation as well as scoring must be available.

Clinical Score	Description
0	No clinical signs
0.5	Loss of tail tone at tip of tail or slight waddle
1	Limp tail or waddling gait
1.5	Loss of tail tone and waddle, or severe waddle with healthy tail
2	Loss of tail tone and waddle, or severe waddle and loss of tail tone at tip of tail
2.5	Severe waddle and loss of tail tone
3	Paresis of two limbs
3.5	Single limb paralysis and paresis of second limb OR paresis of three limbs
4	Full paralysis of both hind limbs
4.5	Full paralysis of both hind limbs and weakness of front limb(s)
5	Moribund, unresponsive to stimuli

Table 1: Example of NCS (EAE) scoring system compiled from various sources.

E. When mice have a limp tail or waddling gait:

   i. Obtain a weight or assess Body Condition Score and NCS at least once weekly.

F. When mice have loss of tail tone and waddling gait, or severe waddle and loss of tail tone at tip of tail:
    i. Daily monitoring should include NCS score and hydration status.
    ii. Animals with decreased skin turgor should receive supplemental hydration-hydrogels or SC fluids.
    iii. Weigh and assess NCS daily.
    iv. Provisions for increasing food and water intake must be made and could include the following: pelleted food on the floor of the cage, moistened food in a dish, supplemental diet.

G. When mice reach paresis of two limbs:
    i. All steps must be continued as above **and**
    ii. Mice must be monitored for dermatitis, urine scalding, penile prolapse, and/or tail lesions. Contact veterinary staff if observed.
    iii. Consider changing to soft bedding only, which can be requested though your vivarium.
    iv. The bladder must be palpated at least three times per week to check for bladder atony.
        1. If bladder atony is identified, affected animals require twice daily manual bladder expression by trained personnel.

H. When mice reach full paralysis of both hind limbs:
    i. All steps must be continued as above **and**
    ii. Animals that maintain full paralysis of both hind limbs and weakness of front limb(s) for more than 24 hours must be euthanized.
    iii. Animals with >20% weight loss must be euthanized unless otherwise approved by the IACUC in the protocol or an approved amendment.

I. Animals with additional evidence of morbidity (e.g., recumbent, poorly responsive or failure to right themselves, abnormal breathing) must be euthanized immediately.

IV. Humane Endpoints

A. Any deviation from the standard UC Davis "Humane Endpoints for Laboratory Animals" Policy, must be described and justified in the approved animal care and use protocol.

B. Additional humane endpoints include:

i. Dermatitis equal to 2 cm^2, or dermatitis with ulceration of any size, or posthitis (penile inflammation), or excessive urine scalding dermatitis. Full rectal prolapse or partial with ulceration/bleeding.
ii. Severe tail necrosis (as a result of the autoimmune response).

C. IACUC-approved deviations from the 20% weight loss humane endpoint.
   i. Because some EAE models may result in transient weight loss >20%, the investigator may request a deviation from this weight loss endpoint. In addition to receiving specific IACUC protocol approval, the investigator must abide by the following:
      1. Animals will be weighed daily and the NCS assessed daily after EAE disease onset.
      2. Animals will be immediately euthanized if body weight loss is >20% for more than 5 continuous days.
      3. Animals will be immediately euthanized if weight loss reaches or exceeds 30% at any point in time.
      4. Animals will be immediately euthanized if any other identified humane endpoint is reached (e.g., dull mentation, minimal or no response to touch).
      5. Campus Veterinary Services (CVS) will be notified daily of the identity and location of animals with >20% weight loss.
      6. If CVS identifies welfare concerns with any animal with weight loss >20%, the investigator and alternate contact will be contacted to immediately euthanize the animals. See "Clinical Veterinarian Authority" policy.
      7. Daily animal weights and NCS assessments must be recorded and records (or copies) made available in the animal room for staff to review at any time.
   ii. Failure to comply with all of the requirements above will result in revocation of IACUC approval for EAE weight loss humane endpoint deviations.

V. Resources

1. West Virginia University "EAE Model Guidance Sheet" https://animal.research.wvu.edu/files/d/60eace26-3966-421d-bb34-f5a0bc8e9ee7/model-guidance-sheet-eae_v1.pdf

2. Experimentica “Refinement of the EAE Mouse Model” https://experimentica.com/scientific_pub/refinement-of-the-eae-mouse-model/
3. Wayne State University " Induction and Monitoring of Experimental Autoimmune Encephalitis (EAE) in Rodents” https://research.wayne.edu/iacuc/eaerodentssop
4. Albert Einstein College of Medicine " Induction and Monitoring of Experimental Autoimmune Encephalitis (EAE) in Rodents” https://www.einsteinmed.edu/uploadedFiles/administration/animal-care-use-committee/Guidleline%20for%20Use%20of%20EAE%20Model.pdf
5. Taconic “Generating EAE Mouse Models of Multiple Sclerosis” https://www.taconic.com/resources/eae-mouse-models-of-multiple-sclerosis
6. UCLA "Care of EAE Mice" https://rsawa.research.ucla.edu/arc/eae-mice/
7. UCSF “Induction and Monitoring Of Experimental Autoimmune Encephalomyelitis (EAE) In Rodents” https://iacuc.ucsf.edu/sites/g/files/tkssra751/f/wysiwyg/STD%20PROCEDURE%20-%20Misc%20Rodent%20Procedures%20-%20Induction%20and%20Monitoring%20Of%20Experimental%20Autoimmune%20Encephalomyelitis%20%28EAE%29%20In%20Rodents.pdf
8. UC Davis IACUC 28 "Humane Endpoints for Laboratory Animals” https://research.ucdavis.edu/wp-content/uploads/IACUC-28.pdf
9. UC Davis IACUC 47 “Clinical Veterinarian Authority” https://research.ucdavis.edu/wp-content/uploads/IACUC-47.pdf
10. Constantinescu, Cris S et al. “Experimental autoimmune encephalomyelitis (EAE) as a model for multiple sclerosis (MS).” British journal of pharmacology vol. 164,4 (2011): 1079-106. doi:10.1111/j.1476-5381.2011.01302.x