

May 4, 2009

Dear Dr. Mellon,

This document summarizes major ACUC concerns with the animal activities of Dr. Michele Basso. The PI has been provided with copies of relevant SMPH and All Campus ACUC minutes at which these and other concerns were discussed.

OLAW-reportable events

- **“Failure to monitor animals post-procedurally as necessary to ensure well-being”**
  - 1/29-2/1/06—Following an experiment, an animal (#96099) was found with obvious CNS signs. Treatment and diagnostics were initiated, including a CT. PI was instructed by vet to check animal overnight 1/30-31—no indication in records that animal was checked that night or the following night. Animal was found dead on the morning of 2/1. Necropsy was performed, but PI removed the brain prior to carcass being submitted, so no cause of death could be determined.
  - 6/19-20/08—During explant surgery, there was screw/drill penetration with some hemorrhage noted during surgery. Animal (#AX25) did not fully recover from anesthesia; research staff was told by vet to call at 10 pm if animal’s condition was unchanged or worse. Last check by research staff at 10 pm indicated that animal was unchanged. Animal was found comatose by animal care staff at 7 am the following morning, propped up in a partially squeezed cage. Euthanized later that day. Necropsy revealed focal subdural hemorrhage. Discussed at SMPH ACUC meeting 7/7, 8/4, 9/8/08. Letter sent to PI on 7/8/08 asking for explanation.
- **“Failure to maintain appropriate animal-related records”**
  - Explant repair ended with animal (#93056) dying under anesthesia on 6/23/03. Although multiple doses of anesthetic were given, there were no records of the times the doses were given. Discussed at 10/3/03 SMPH ACUC meeting.
  - 6/19-6/20/08—Research staff observations were not recorded in the animal’s (#AX25) records, but rather in the lab notebook, which is inaccessible to veterinary staff after business hours. PI stated in ACUC meeting of 8/4/08 that the students chronically do not write in the records despite being told to do so, and that PI does not know how to correct this issue.
  - Animal (#1640) was inadvertently left in play cage overnight. While there were no ill effects, the incident was not recorded in the animal’s record. Discussed at SMPH ACUC meeting 8/04/08.
  - PI repaired skin after explant became dislodged. Records of the anesthesia and repair were not available in the animal’s (#AX25) record for a week

after the procedure. This occurred after ACUC-mandated records training. Discussed at 11/3/08 SMPH ACUC meeting.

- **“Failure of animal care and use personnel to carry out veterinary orders”**  
(note: UW-Madison’s PHS Assurance includes the Chancellor’s Memorandum on Veterinary Authority)
  - On 4/8/04 PI performed a clinical assessment of an animal (#97098) doing poorly, and ordered a CT scan without consulting a veterinarian. PI then challenged the authority of a veterinarian who refused to allow the animal to be moved after the CT scan due to its unstable condition and who had ordered a necropsy. PI called the IO, the LAR director, and the ACUC chair to dispute the vet’s decision. Discussed at SMPH ACUC meeting 4/19/04. Letter sent to PI 5/04. PI requested letter be retracted; ACUC declined to do so.
  - In 1/05, animal (#97090) with CNS signs was treated with dexamethasone. After lengthy consultation with veterinary neurologist, MD anesthesiologist, and MD neurologist, it was decided that dexamethasone was contraindicated. Despite veterinary instructions to the contrary, PI treated animal with dexamethasone. This is documented in the animal’s medical record.
  - 6/19-6/20/08—After explant surgery, animal (#AX25) was recovering poorly. Veterinarian instructed research staff to call if animal’s condition remained unchanged or worsened. Animal was found comatose the next morning; vet was never called. Discussed at SMPH ACUC meeting 7/7/08, 8/4/08, and 9/8/08.
  - On 10/13/08 PI repaired skin (animal # 1640) after explant became dislodged, and did not call a veterinarian before beginning repair, as required by the SMPH ACUC. PI also did not notify veterinarians that the repair was healing poorly, due to haired skin that was curled into incision—it was discovered during a routine walk-through. Repair was re-done by veterinarian, after explant replacement surgery had to be postponed. Discussed at 11/3/08 ACUC meeting.
- **“Failure to adhere to IACUC-approved protocols”**
  - PI started a post-operative animal (#1640) on water restriction prematurely (too soon after surgery). Discussed at SMPH ACUC meeting 8/4/08.
- **“Conditions that jeopardize the health or well-being of animals”**
  - Animal (#R99045) reported ill 8/11/03 with CNS signs, died 8/23/03. Necropsy revealed large left frontal lobe abscess, with penetration of the brain by screws in both the left and right frontal regions.
  - Explant applied 7/24/03, animal (#R98054) reported ill 9/11/03 with CNS signs, euthanized 9/13/03. Brain CT on 9/12/03 indicated possible abscess and screw penetration through dura, although CT report is not in medical record. Animal not submitted for necropsy.
  - After experiment on 1/12/05, blood was visualized on probe after it was withdrawn—cerebral hemorrhage suspected. Animal (# 97090) recumbent, taken for brain CT 1/13/05, died during scan. No CT scan

report available. Animal, without brain, submitted for necropsy. Unable to determine cause of death.

- After experiment on 1/28/06, animal (#96099) was found recumbent in cage on 1/29/06. CNS signs present, including seizures. Cerebral swelling evident on visualization of cylinders. MRI performed 1/31/06. No MRI report in record. Found dead in cage 2/1/06. Animal submitted for necropsy; brain observed grossly by veterinary pathologist, but despite multiple calls, PI did not contact pathologist when the brain was sectioned, so no internal dissection or histopathology was done.
- Purulent discharge from explant first noted on 8/15/03, after eye coil replacement on 7/24/03; animal (#96089) was on antibiotics almost continuously until euthanasia at end of study on 5/5/06. Animal was not submitted for necropsy, so cause of infection is undetermined.
- Starting 4/24/02, an animal (# 96089) was noted to have 9 eye coil replacement surgeries, with the last one being 4/21/06. Despite multiple instances of eye coil failure, the PI sought no assistance until pressured by the SMPH ACUC. The last two surgeries were done with specific ACUC permission, after specific protective interventions were required. Discussed at SMPH ACUC meeting on 11/1/04, 12/6/04, and 3/7/05.
- In response to a standard question during protocol review in 1/09, it was discovered that the PI was using non-sterilized probes, rinsed with tap water, to penetrate the dura and perform physiological readings. When told this was inappropriate, PI replied that, "It is my understanding that tap water is sufficiently chlorinated to kill off any bacteria otherwise it would be unsafe for our consumption". PI then asked for references from reviewers to illustrate their concerns about this practice. (Note: not yet included in minutes, but documented by emails sent by PI.)

## Summary

This PI has had significant difficulties with the cranial explant model—many more than other investigators using the same model in the same animal care unit with the same veterinary staff. There is a lengthy history of non-cooperation with veterinary staff, including failure to follow explicit instructions and reluctance to permit necropsies on animals that die with CNS signs. There have been multiple instances of proven or suspected brain abscesses, and multiple events involving screws penetrating the dura, leading to either hemorrhage or abscess. Animals have been left unattended for hours in compromised condition—the most recent event in June '08 is what triggered the involvement of the All Campus ACUC. Medical records are often incomplete or inaccessible; despite training, PI insists that it is unclear what needs to be recorded in a medical record. Recently it was discovered that the PI has been inserting unsterilized materials into brain tissue. This could be a partial explanation for abscessation and chronic inflammation that has affected several research animals.

Sincerely,

Janet Welter, DVM, MPH, PhD, DACLAM  
Chief Campus Veterinarian