**IACUC Training Exercise #3 – 2019 (Thoughts about tethering)**

The following exercise may be useful in stimulating discussion regarding compliance with PHS Policy and VA Handbook 1200.07. To facilitate discussion, page 1 of the exercise may be distributed to the IACUC members prior to a meeting. After a few minutes of discussion about the exercise during the meeting, the remainder of the exercise may be distributed to provide ideas for the committee’s consideration.

The Hometown VAMC IACUC is reviewing a new protocol submitted by Dr. Charlie Greene, a neurologist who studies epilepsy. Dr. Greene has just been awarded funding for a new system for continuous recording of electroencephalographic (EEG) signals from rats (<https://bmcneurosci.biomedcentral.com/articles/10.1186/s12868-019-0490-z>) allowing him to record brain activity before, during, and after seizures, which is essential to advancing his research to treat and prevent seizures. Previously, he had tried using wired systems to obtain EEG recordings but the disadvantages (wire breakage, electrode connection issues, animal health complications) outweighed the advantages (e.g. lower cost, ability to simultaneously record from a large number of electrodes). Dr. Greene also looked at wireless EEG recording systems; although more stable than wired systems, they were very expensive, which limited the number of animals that could be observed at one time. The new system that Dr. Greene will be setting up represents the best of both worlds. The implanted electrodes are connected by a cable to the recording equipment, but the connections involve swivels that allow the rats to move freely in both the horizontal and vertical planes, and a counterbalancing system that takes up the slack in the cable, so that it stays out of the way and is protected from being chewed or otherwise damaged by the rat.

In his ACORP, Dr. Greene described the new system as allowing the instrumented rats to move freely about the cage, which is also much larger than the standard rat cages. But when the IACUC met, Sperry Blackburn, Non-Scientific Member and a lawyer specializing in elder abuse and neglect, said Dr. Greene’s new system looked to him like a form of “restraint” because the rats were in fact tethered by the cable that is fixed to the recording equipment. Several other committee members wondered if the rats would be “distressed” by being tethered and whether such restraint would be considered a departure from the *Guide*.

What are your thoughts about tethering?

The *Guide’s* definition of physical restraint found on p. 29 is “the use of manual or mechanical means to limit some or all of an animal’s normal movement for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation.” The *Guide* also specifies that “animals must have enough space to express their natural postures and postural adjustments without touching the enclosure walls or ceiling, be able to turn around, and have ready access to food and water.” (p. 56). In keeping with the space considerations noted on p. 56, the *Guide* on p. 29 recommends that restraint devices be designed, sized, and operated in a manner that minimizes discomfort, pain, and distress to the animal. Finally, the *Guide* (p. 29) states “Prolonged restraint, including chairing of nonhuman primates, should be avoided **unless** it is essential for achieving research objectives and is specifically approved by the IACUC (NRC 2003b).” Dr. Greene’s new EEG recording system, featuring a double swivel and counterbalance arrangement, allows the rats to move freely in all dimensions; therefore, the cable does not limit the rat’s ability to make normal postural arrangements. Even if the IACUC decides tethering as described in this example is a form of restraint, it would not be a departure (note: the bolded **unless**) if approved by the IACUC, because the use of the new EEG system is essential to Dr. Greene’s research and was so noted in his ACORP. Based on this information, the tethering would be a deviation from a “should” statement, according to a specifically established exception in the Guide (experimental reasons). Exceptions are not departures from the Guide and have no reporting requirements. Information about *Guide* deviations and departures is available at <https://www.research.va.gov/programs/animal_research/required_training.cfm>.

If the IACUC has any lingering doubts, the IACUC could choose to approve just a pilot study first, involving a small number of rats, which would allow the committee to observe firsthand the rats tethered to Dr. Greene’s new EEG recording system and then determine the appropriate pain and distress category assignment. Dr. Greene may also want to provide the IACUC data showing that the rats maintain their body weight and do not display common rodent indicators of pain and distress (e.g. porphyrin discharge, unkempt coat, lethargy, etc.). If the IACUC concludes that this type of tethering is not distressing to the rats, then category D would be appropriate since the rats have undergone a survival surgical procedure and received postoperative analgesics. Should some rats not adapt to Dr. Greene’s tethering system, Dr. Greene’s ACORP specifies that those animals will be removed from the study; that makes category E assignment unnecessary because withdrawing those animals from the study relieves the distress.