

Q17a – Since the plans now include multiple experiments on the same animal, two points need to be added here; 1) the actual flow of procedures for each study (i.e., blood draws, laser imaging, EMG, and MNCV) and 2) a description of the maximum number of studies that will be done on any one animal.

Q19 – Please state the possibility that exposure to SEAP, Gaussia, or Metridia could cause an anaphylactic response and what the treatment plan will be if this occurs.

Q20 – Please elaborate on the details regarding why multiple injections into the same limb should not create any chronic long term effect.

M01640-3-08-06 (Basso) Renewal

Physiological underpinnings of movement disorders in nonhuman primates

Primary review by Abbott/Capuano. Abbott/Sandgren moved to approve pending response to the committees questions. Discussion ensued. The committee voted 1 yea, 6 nay, the motion failed. Abbot/Capuano move to defer until extensive revisions are made and the protocol is brought before the full committee for additional review. More details are needed for experiments and timelines. The committee did not find problems with the procedures, however there is concern regarding the lack of details. Extensive veterinary consultation is needed prior to this protocol being rewritten. The vote was unanimous.

The Graduate School ACUC will share their questions with the Medical School ACUC and recommends to the Medical School ACUC to consider the risks associated with proper PPE in a room that does not have a solid animal barrier.

Q8 - Sentence in second line of second page should read: 'Ketamine or an anticonvulsant such as Benzodiazapine or an equivalent.'

Q11a - A more widespread use of lay language is required. Avoid terms such as "dystonia", "subclavically" and "visuomotor task electrical activity".

Q11a – Anatomical studies are referred to in this question, however, Questions 9a and 12 do not refer to animals that would be used for anatomical studies. Please clarify. Will perfusion be used? Would it otherwise be required? If not, then perfusion must be discussed in this protocol and the number of animals used for this must be accounted for. Q9a/12 - Provide details of "statistical criteria" showing that only three animals per group are required. Since the PI mentions that more than three animals per group will be required if there is significant inter-subject variability, such an allowance must be made in the number of animals requested.

Q16b - Biohazards. [REDACTED] PPE will have to reconcile with [REDACTED] PPE. Unless the animals are in a room separated by a solid barrier from the laboratory, personnel must maintain protective clothing when rhesus monkeys are present. Changing gloves to operate computers or equipment, or temporarily covering PPE with a clean lab coat for such a purpose, is no issue. A lab coat and scrubs should be worn.

Q17a - Eye movement recording. Judge et al, 1980 is not attached (neither are materials for Anatomical Markers, below). In addition, individual procedures are described, but a description of specific experiments performed on each animal, including a timeline, is needed here. For example, in each experiment what will be the maximum number of times each procedure will be given to each animal? In what order will the procedures be given? What minimum duration will occur between each procedure? Et cetera. Include any training time periods in each timeline.

Q17a - Electrical stimulation. Provide details of the electrical stimulation used, including maximum values, duration and numbers of repeated stimulations in any single stimulation session. What will be the maximum number of stimulation sessions each individuals receive and at what minimum interval?

Q17a - Microinjections. Provide details of doses, volumes and liquid vehicles used, including maximum values, frequency of administration to individual monkeys, and minimum intervals between administration. Provide details of how brain lesions are made using electrical or chemical means (such as using ibotenic acid, including sources, purity/quality if known), and include how many lesions per animal will be made, in which brain locations. Scientifically justify each one.

Q17a - Anatomical markers. Details of dose, volume, vehicle used and brain locations need to be given for brain marker infusions (and sources, purity/quality if known). Provide details about "small currents" used to induce "marker lesions". A whole series of anesthetic agents are given here without mention of dose, route of administration and any repeated dosing that may be necessary. In this complex protocol, it is too confusing to try and match up anesthesia procedures in the surgical section with procedures described here. The anesthesia details need to be given here as well as later in the protocol (this applies to all relevant section in Q.17a.)

Q17a - Under the heading of ROUTINE WOUND CARE AND MAINTENANCE there needs to be more complete and explicit cleaning procedures described for cylinder chambers. Saline and povidone iodine flushes alone will not discourage the growth of bacteria inside the chambers.

Consultation with a veterinarian is recommended to implement a rotation of antibacterial flushes for cylinder chambers that will reduce the numbers of bacteria and maintain them at a minimum.

Q17b - Provide anesthesia details. Provide details about the progression and frequency of collar and pole training and about the frequency of recorded observations while animals are in the chair.

Q17b - Please describe how the animal's hands will be kept away from the head area during restraint.

Q17c - The parameters for fluid restriction need to be well-defined.

The stated amount of weight loss at which the monkey will no longer be fluid restricted is 15%, but there is no stated parameter for the originating body weight. Or put more simply, 15% of what?

Q18 - Address the need (or lack of need) for analgesia with regard to peri-orbital implants and eye-related surgery.

Q19 - Describe how frequently an animal's condition is recorded via infrared camera monitoring.

Q20 - Any brain manipulation carries a high risk of complication. Please describe here, or consult with a veterinarian the scenarios that should be considered here.

Q24 - Please include the relevant veterinarian in surgical training and approval.

Q27 - Due to the variety of anesthesia described, link anesthesia with specific procedures here.

Q27 - Recommend removing pentazocin from the list of approved analgesics because it is not very effective.

Q28 - There is no description of the procedure for removing excess granulation tissue from the dura in the cylinders. Please provide that information here.

Q28a - In addition to describing the various surgical procedures, please provide a timeline of surgical procedures experienced by individual monkeys during each experiment.

Q28a - Cylinder implant. Delete repeated sentence starting, "Trephoning is periodically interrupted....". Provide details on dimensions, weight and material construction of the cylinder implant. Describe the cap and how it is sealed on to the cylinder. How is the cylinder prevented from moving: does the bone wax hold it in place or is cement used?

Q28a - Explant construction. Provide a diagram illustrating progressive stages or the completed procedure. It is unclear where everything is positioned in this procedure. Describe the dimensions, weight and material construction of the eye coil connector and cylinders.

Q28a - Stimulus generator device implant. Describe the dimensions, weight, and material construction of the deep brain stimulating electrodes and where in the brain they will be placed. How is this brain area exposed?

Q28a - MPTP injections. Describe the source and quality of the MPTP.

Q28a - State the maximum number of times repairs for each preparation will be performed and justify that this number of times does not compromise the animal. Where appropriate, describe the surgical procedures to remove each implant.

Q29 - Describe the minimum frequency of observation of animals post-surgically.

Q30 - List the number of animals to be given each combination of surgical procedures. Make it clear in Q28a that which are combined and which are separate surgeries. What will be the minimum delay between cylinder implants? Please provide surgical details regarding the implantation of the second cylinder in Q28a.

Q35a - Provide details here about the duration of experimentally-required individual housing.

Q35a - Please state that the animals functionally speaking do indeed require individual housing since they are all fluid-regulated.

Attending Veterinarians' Report

Dr. Krugner-Higby reported that per the committee's request following review of a protocol last month, she met with a PI to discuss the use of self-reinforcing compounds. The meeting went well and a rewrite of the protocol is expected.

Dr. Krugner-Higby stated that she spoke with another PI regarding the use of implantable pellets for drug delivery rather than multiple IP injections. That PI was amenable to the suggestion.