Institutional Animal Care and Use Committee
12/28/2020 Minutes
VCRC - 76D

Meeting Convened: 12:18pm	Quorum Requirement: 10
Meeting Adjourned: 2:10pm	Members Present to Vote: 12

Voting Members			Alternates		
1		(Chair - M, S)			
2	X	(Vice-Chair - M, S)			
3			A	X	(A, S)
			B		(A, S)
			C		(A, S)
			D		(A, S)
			E		(A, S)
			F		(A, S)
			G		(A, S)
			H		(A, S)
4		(M, S)	I	X	(A, S)
5	X	(A, U)	J		(A, U)
			K		(A, U)
			L		(A, U)
			M	X	(A, U)
			N	X	(A, U)
6		(M, S)	O	X	(A, S)
7		(M, V)	P	X	(A, S)
8		(M, S)	—		
9	X	(M, S)	Q		(A, S)
10	X	(M, S)	—		
11	X	(M, S)	R		(A, S)
12		(M, S)	S		(A, S)
13		(M - NA, NS)	T		(A - NA, NS)
14	X	(M, S)	U		(A, S)
			V		(A, S)
15		(M, S)	W		(A, S)
16		(M, S)	X	X	(A, S)
17	X	(M – St)	Y		(A, St)
			Z		(A, St)

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii		(O, U)
iv		(O, U)
v	X	(O, S)

Institutional Veterinarian:

3		(M, S)

Correlates to Version **v2.98** of the IACUC Roster

M = Member, A + Alternate, S = Scientist, NS = Non-Scientist, NA = Non-Afiliated, V = Veterinarian, St = Student, O = Ex-officio, U = University Staff

Discussion/Information Items:

- The committee was updated on a new policy from Occupational health that will required annual renewal for the Animal Exposure Questionnaire (AEQ). The change is in large part to help identify individuals who are developing animal allergies earlier, as earlier identification can aid in interventions to prevent animal allergies from progressively worsening. Early identification is especially important at an institution like the UMN where we do not require PPE and respirators for all interaction with rodents which is used at some other institutions to prevent laboratory animal allergies.
- The committee was updated on an incident where a lesion was identified on an animal that had recently undergone a surgery and subsequent imaging procedure. The area veterinarian and UMN veterinary staff are working closely with the lab to diagnose and prevent future incidents. The committee will be updated as these efforts continue.
- The committee received a self-report in which an emergency pericardiocentesis was performed by experienced surgeons on a study. The protocol has been updated to include this procedure and the area veterinarian has consulted with the lab regarding future treatments. The committee had no additional comments.
- The committee discussed an incident where a lab had complications following tail vein injections. The lab staff will undergo mandatory retraining for proper tail vein injection technique from the veterinary staff. The committee will be updated on these efforts at a future meeting.
- The committee was updated on ongoing efforts to assist a lab that had a recent incident following tamoxifen injections. Results from the tamoxifen culture were negative. The lab will work with the area veterinarian to provide additional training and feedback during the next procedure involving tamoxifen injections.
- The committee discussed a protocol review scenario that was recently published in Lab Animal (Lab Animal IACUC Scenario).

  The scenario outlined a fictional case where institutional veterinarians discussed as a group the pain management outlined on a NHP study where animals would receive cranial implants. The investigator in the scenario did not include the veterinarian recommended analgesic regimen in the protocol and cited only anecdotal observations and past performance as a rationale for not including the multimodal pain management approach. The IACUC in the scenario then approved the protocol without the recommended analgesic regimen.

  During discussion the committee identified the following topics as concerns in this scenario:

  - The veterinarian's suggestion was based on consultation and agreement with the other institutional veterinarians and as subject matter experts should be implemented in the protocol unless scientific justification is provided to reject the recommendation in favor of another analgesic regimen. In an instance where there was not a consensus among veterinarians, there may be more room for discussion, but in this scenario it states that the institutions veterinarians were in agreement on the pain management recommended.
  - While the PI in the scenario provided a rationale for not implementing the veterinarian's recommendation, it was not a scientific justification. If the committee is to approve the

altered pain management plan, a scientific justification needs to be provided beyond anecdotal observations.

- Improved communication between the veterinarians and the investigator could help this interaction. For example, a fact based conversation between the veterinarian and the investigator outlining the advantages to the pain regimen and information about the multi-modal approach being modern standard practice may have facilitated implementation of the recommendation.
- As research and standards evolve, methods that have been previously acceptable may need to be altered. To facilitate these changes, increased communication between the committee, veterinarians, and investigators with details describing the rationale behind the new standards is very helpful in avoiding conflict and helping to ensure acceptance of and compliance with new standards
- NIH-OLAW and USDA-APHIS both agreed that "scientific justification in writing by the investigator" is required if the veterinary recommendation pain management or animal care will not be followed. In addition the USD –APHIS response stated:

> *"The IACUC does not have the authority to prescribe methods or set standards of design, performance, or conduct of research, but they have the authority, and the responsibility, to require modifications to secure approval or withhold approval of a proposal when procedures are not performed with adequate analgesics or anesthetic, or when no scientific justification for withholding analgesics is provided."*

1. **IACUC-NEW (# Protocols: 4)**

1. **Protocol Title:** 2001-37746A Hearing and Sound Communication in Frogs
Species &Pain Class: (A,B,C) Amphibian (Other)
Question the Research Addresses: This research program seeks answers to the following questions about frog communication: how do their vocalizations evolve, how are they used to make adaptive behavioral decisions, and what are the biophysical and physiological mechanisms that underly auditory perception and decision making?

   The committee concurs that this protocol can be approved via designated member review once the following stipulations are addressed by the PI:

   - Will all species of frogs encountered in the field be collected? If multiple species may be used, please point out any modifications to "standard" frog housing to accommodate species specific requirements. IMHA Section: - Are temperature, humidity, and photo period requirements known or standardized for the species used? Are temperature and humidity monitored or controlled (beyond building standard)? What is the light cycle in the IMHA? Do you ever verify/confirm lights go on and off at appropriate times? Does this species require full spectrum lighting? - IMHA #14: you state animals are fed 6-9 crickets per week. Please provide clarity on the schedule of feeding. Are 6-9 crickets offered once/week? One to two crickets each day? Animal numbers: You are requesting the same number of animals as the last version of this protocol. How many animals were used in the last iteration? Are you requesting the same number to repeat work done in the last 3 years?

   - Please clarify why field tested animals require identification/toe clipping.

   - Overnight courier: You describe shipping up to 4 individual containers in a single cooler, with ventilation holes in the cooler. Are ventilation holes also made in the primary containers, or the shipping box? Anecdotally, do animals generally tolerate shipping by this method well? (E.g. low

mortality, animals arrive in good health and perform as expected in behavioral tasks).

- I am unable to determine final injection volumes with the calculation you provided. Please provide the average body weight of a female frog and clarify which mass units are used in your calculation (oz, g, other) or list maximum volumes administered in a single injection for each hormone. (The primary concerns is IM injections in to the small muscle mass of a frog). Your description (and logic) suggest you must dilute drugs to appropriately dose small animals. If so, please describe how you ensure sterility of final product (use of sterile amphibial saline? Filter? Other?). Please provide a brief description of amphibian saline.

- Cardiac puncture is recommended only as a terminal procedure under anesthesia in other laboratory animal species. Please justify why a survival blood draw is necessary, why anesthesia cannot be used, and why cardiac puncture was chosen over other blood collection methods.

- Please clarify why 40 frogs will be transferred internally. Are they different from frogs collected from the wild?

- You state multiple drugs and dose ranges are included as options to account for interspecies availability, but do not describe which species you are using, which drugs and doses are used for which species, or a process of optimizing drug and dose for any species. Please clarify these points. You have included 2 paralytic agents. One of them - tubocurarine - is generally not used in human or veterinary medicine due to the availability of pharmaceutical grade alternatives that are deemed safer. Please justify why this drug is desirable for your procedures. Please provide the maximum IM volume a frog may receive in a single injection. IM is strongly discouraged in small animals due to complications of injecting into miniscule muscle masses (pain, inflammation, muscle necrosis). RAR does not have volume guidelines for amphibians, but the guidelines for small mammals is 0.05 ml of injectate per kg of body weight per injection site. Are you able to conform to these guidelines if IM injections are critical? The purpose of monitoring immobilized animals is to ensure their physiologic stability. Please describe how you will monitor the animals biological function - not just the degree of immobility.

- You list a number of manipulations (inflating lungs, blocking eustacian tubes, coating animal in vaseline) but do not describe whether and how these affect the animal's physiologic state. You also do not provide details about how long these manipulations may last, or how they are accomplished or reversed (with the exception of lungs). Please provide descriptions of how these manipulations occur, how animal physiologic state is monitored and maintained during them, and how these manipulations are reversed. I was able to access some (not all) of the references you provided regarding immobilization. Of the papers I read, there are not data to support the claims of stable and normal heart rates in the absence of painful stimuli, nor are there descriptions of the painful stimuli. I did not find descriptions of the manipulations listed here either, and whether or how heart rate changes. Please discuss the degree of expected distress animals may experience during these extended manipulations, with references when possible.

- Is the skin overlying the craniotomy site closed (sutures, glue, other)? Lidocaine is not expected to provide analgesia of adequate duration, and its effect on pain associated with the bone manipulation (as opposed to skin incisions) is unclear. Please contact your RAR veterinarian to discuss analgesia options.

- Please clarify the redosing schedule for this procedure (expected to last up to 8 hours, but immobilization procedure only lasts ~3). Clarify all probes, dyes, and instruments used are sterile. Please describe how animals are monitored for pain or physiologic perturbations during this procedure. Please explain how the skin overlying the craniotomy site is opened for access, and closed after recording.

- Can blood be collected immediately after euthanasia as opposed to immediately before?

- Please update your responses to questions 1-3 to include likely adverse events from all of the procedures proposed.

Committee Decision: Stipulations must be met
For: 12 Against: 0 Abstain: 0

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2. **Protocol Title:** 2001-37774A A Preclinical Study to Evaluate Mitral Technology in the Sheep Model.
Species &Pain Class: (B) Sheep (Biomedical)
Question the Research Addresses: Animals will be used to evaluate the biocompatibility, functionality, and durability of a developmental heart valve.

The committee concurs that this protocol can be approved via designated member review once the following stipulation is addressed by the PI:

- The post operative care section for RAR should contain the carprofen that will be administered in the post operative period. Regular buprenorphine for any breakthrough pain has also been commonly used for these procedures. Please add if this is the plan.

Committee Decision: Stipulation must be met
For: 11 Against: 0 Abstain: 0
Member 11 out

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3. **Protocol Title:** 2001-37768A Spectroscopic and Electrochemical Studies of Immune Cell Communication
Species &Pain Class: (A,C) Mice
Question the Research Addresses: How does cell-cell communication change in different environments? Howcdoes malaria change the way the immune system reacts with it and other immune cells.

The committee concurs that this protocol can be approved via designated member review once the following stipulations are addressed by the PI:

- Please update the following: - Please update the protocol to provide additional detail on frequency of increased monitoring following onset of clinical signs (2x/day, 3x/day?). - There are discrepancies on the endpoint - in Health and Monitoring, it states up to 20 days post infection, while Experimental Endpoints states 10 days. Please update to reconcile this discrepancy. - Please update to indicate additional supportive care that could be given to mice exhibiting clinical signs (parenteral fluids, heat, etc.) in addition to moistened feed. - It is a bit unclear when sick animals will be euthanized. In one place it states within 24 hours but in another it states that if blood levels are not in desired range animals will be kept alive. Please clarify if you are looking for blood levels of organism to be anywhere between 5-50% for all mice or if some need to be at the the higher concentration before euthanasia. If there will be separate groups for different infection levels, please also update the Experimental Design to outline these groups.

- Additional correspondence with the lab indicated that you have not had issue of animals being extremely sick with major weight loss before hitting the high 50% infection level. If so, please consider updating the protocol to remove the request for moribundity as an endpoint.

- We are unable to confirm [redacted] has completed the Animal Use Tutorial. Please follow up with [redacted] to ensure this requirement is completed. Once complete, please confirm here in eProtocol.

Committee Decision: Stipulations must be met
For: 12 Against: 0 Abstain: 0

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4. **Protocol Title:** 2001-37754A An Acute Porcine Sepsis Protocol for Evaluation and Development of a Novel Noninvasive Vascular Pressure Sensor
Species &Pain Class: (B) Pig (Biomedical)
Question the Research Addresses: This study aims to determine whether changes in a peripherally transduced venous signal over time can predict intravascular fluid status is guiding real-time sepsis resuscitation.

   The committee concurs that this protocol can be approved via designated member review once the following stipulations are addressed by the PI:

   - Although there is not a grant proposal associated with this study, please update the specific aims section of the Rationale to further describe the experimental goals. Please include more detail on what the sensor is doing and what the data will be used for.

   - It currently says that vital signs will be recorded every 30 minutes. However, heart rate, respiratory rate, temperature, and mean arterial pressure should be recorded at least every 15 minutes, per IACUC policy. This will need to be changed in the attachment as well. Pressor Resuscitation: Says that norepinephrine will be given "until MAP of 65 or 5% of initial pressure (whichever value is higher), and then until MAP is within 5% of initial." Please re-word to make this less confusing. The numbers justification explains that 12 animals are needed "to develop a usable algorithm". Please expand on how it was determined that 12 animals are necessary for the algorithm. Since this was listed under the "Product Testing" heading, please also clarify which agency provided the guideline to use 12 animals. If this study is not Product Testing, please move the numbers justification to another heading (such as Pilot or Other).

   - It says the blood sampling will occur approximately every 15-30 minutes and then it says maximally every 30 minutes during the procedure. Please reconcile.

   - In the procedure description, it says that "after imaging, animals may be administered heparin...". Please change to "After procedure is complete...", since imaging will not necessarily occur. The training and experience section for Matt Lahti talks about percutaneous aortic valves. Please replace this with information that is relevant to this specific procedure. Aside from emergency use, is amiodarone needed for this procedure? It is listed as being administered during the implant procedure, but there is no implant. Under the parameters being measured and steps taken sections, there are references to paralytics. Please remove these as paralytics are not being used in this procedure.

   - We are unable to confirm Roy Kiberenge has completed the ROHP online trainings and tetanus requirement. Please follow up with Roy to ensure these requirements are completed. Once complete, please confirm here in eProtocol.

   Committee Decision: Stipulations must be met
   For: 11 Against: 0 Abstain: 0
   Member 11 out

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2. IACUC-AMENDMENT (# Protocols: 0)