Institutional Animal Care and Use Committee

6/1/21 Minutes

VCRC - 76D

Meeting Convened: 12:01 PM	Quorum Requirement: 9
Meeting Adjourned: 1:26 PM	Members Present to Vote: 13

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v4.0** 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

1. The committee reviewed an adverse event report involving an animal that died following anesthetic induction for a surgical procedure. No specific cause of death could be identified. The lab will continue to follow best practices for anesthesia and monitoring. The committee endorsed the plan and has no further concerns at this time.

2. The committee reviewed a self-report in which unapproved imaging procedures had been conducted over a period of time. An amendment has been submitted and approved to add the procedure to the protocol. The committee requested additional information on the publication status of data obtained from the unapproved imaging and will be updated at a future meeting.

3. The committee reviewed a self-report in which tail lesions that did not require amputation or analgesics were found on animals that had undergone surgery. The lab will begin using heat support throughout the surgery as required, in addition to the current heat support during recovery. The committee considers the matter closed.

4. The committee discussed the length of time to allow for review of protocols. Committee members were reminded to contact the chair if they are not able to complete their reviews in a timely manner, to allow for reassignment to another reviewer. If an investigator has not responded to comments or taken other action on a pending protocol for at least four months, the office will contact them to give a one week deadline. If no response or action is taken, the protocol will be returned to the PI and would start a new review cycle if resubmitted.

5. The committee continued the discussion from a previous meeting on sourcing of NHPs. RAR will continue to enforce their policies, and the IACUC will develop a broader policy to be considered at a future meeting.

1.

1. **IACUC-R1S1(# Protocols: 13)**

    1. **IACUC-R1S1 - NEW(# Protocols: 9)**

        1. **Protocol Title:** 2104-39037A Identifying long-range polarity cues using spontaneous mutations in mammals
        Species &Pain Class:(A) Guinea Pig; (A) Mice
        Question the Research Addresses: This research will uncover novel mechanisms that control the orientation of cell behaviors during embryogenesis.

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

            Comment: Typically, a consent form describing the study, the procedures involved and risks to the animals is required to be signed by clients prior to enrollment. A template will be sent via email, please update to fit your study and attach an unsigned version to the protocol.

            Comment: For aim 3a/ 3b, will any of the mice in 3b be exposed directly to samples from the Guinea pigs or is there any chance samples will enter a vivarium? Or will you just be genetically engineering the mice using CRISPR based on the mapping from aim 3a?

            Comment: Please include some additional information regarding how samples are transferred [redacted] and how they are handled in the [redacted]? Due to potential for pathogen transmission to animals in the vivarium from [redacted] guinea pigs, it is recommended to handle these samples within a biosafety cabinet. Additionally, on days when samples are collected, will those lab members be in contact with any animals at the university? Lab members should not enter a vivarium after working with the [redacted] animals without changing clothes.

            Comment: While there are no anticipated health concerns for the guinea pigs from a cheek swab, in the event of an injury, please include a statement that the guinea pig will be brought to a veterinarian designated by the [redacted] or owner.

            Comment: In the Guinea Pig section of health and monitoring, you state "We do not except adverse reaction to

procedure." I believe you mean to say you do not expect any adverse reactions. Please update the wording.

Comment: How will you limit liability to the University with the client-owned/[redacted] guinea pigs? Will you have owners sign a waiver of some sort? If so, please ensure University council has reviewed and approved such a waiver. This could also be addressed in the consent form.

Comment: Euthanasia is needed for fetuses greater than e15 days. Please update the protocol to include the method for euthanasia of fetuses at e. 15.5 day needed for your study. Decapitation is the recommended method.

Committee Decision: Stipulated
For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 2104-38974A Novel Theranostics for Solid Cancers
Species &Pain Class:(A,B,C) Mice; (A,B,C) Hamster
Question the Research Addresses: The combined therapeutic effect and imaging capability of the oncolytic adenovirus (OAd) expressing the sodium iodine symporter (NIS) and Interferon alpha (IFN), will be analyzed in murine and hamster cancer models.

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

   Comment: At the top of the experimental design summary table, please adjust where it says "a total of 340 animals (260 mice and 180 hamsters) are required for this study", as the species section and table both request 295 of each species for this study.

   Comment: In the list of experimental endpoints, it is noted at #2 that one endpoint is a tumor in mice whose volume exceeds 2 cm^3. Will a tumor size-based endpoint also be implemented for hamsters, and if so, what will the endpoint be? Please update the protocol if needed.

   Comment: Please update the protocol to clarify if the intratumoral adenovirus injection in hamsters is to be performed under anesthesia or without anesthesia. Intratumoral injection with adenovirus is described in the procedure "adenovirus injections in hamsters (ip)", which is listed as a procedure not using anesthesia, and is also described in the procedure "Intratumoral and IV injections with adenovirus in hamster", where it is described as a procedure that will be using anesthesia.

   Comment: The investigator proposes to duplicate studies in both mice and hamsters. Since it is well documented that mice do not allow a permissive environment for oncolytic adenoviruses but hamster do, please update the protocol to provide more specific reasons for the necessity of the mouse studies. What critical information can be provided by the mouse model that cannot be provided by the hamster model?

   Comment: Although the investigator has provided general details as to what the experimental flow will be, we do not know specific details as to how the studies will be carried out. Please provide details as to the procedures and time line associated with a typcial study; perhaps a flow chart outlining the course of the experiment.

   Comment: Please update the protocol to explain what role the surgical resection of tumors in hamsters will play in the overall experimental strategy.

   Committee Decision: Stipulated
   For: 13 Against: 0 Abstain: 0

3. **Protocol Title:** 2104-38980A Veterinary Clinical Skills Program: Large Animal Training
Species &Pain Class:(A,B) Horse; (B) Cow (Biomedical); (A) Goat; (A) Other; (A) Other
Question the Research Addresses: N/A

   Committee Decision: Approved
   For: 13 Against: 0 Abstain: 0

4. **Protocol Title:** 2103-38932A Novel procedure development, surgical skills and support training, and nonhuman primate tissue donation
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: This protocol is intended to maximize the contribution of NHP

subjects ineligible for long term research protocols. A subset of animals used in our approved protocols complete research objectives meeting the study endpoint, but are ineligible for (re)enrollment on chronic long-term studies. This is especially the case in which an animal has received a biologic therapy (e.g. monoclonal antibodies, gene therapy, targeted immunotoxin) that limits the potential to meet stringent inclusion criteria for long term studies. Other rare situations include animals that have met exclusion criteria during evaluation and preparation on our enrollment protocol.

Committee Decision: Approved
For: 13 Against: 0 Abstain: 0

5. **Protocol Title:** 2105-39060A Role of PKD in right ventricular dysfunction during pulmonary arterial hypertension
Species &Pain Class:(A,B,C) Rat
Question the Research Addresses: The proposed studies aim to test whether PKD inhibition at the mitochondria can mitigate the development and progression of right ventricular dysfunction and fibrosis in a preclinical animal model of PAH.

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

   Comment: Since hypoxia can induce respiratory distress and labored breathing as mentioned in question 1, please state in question 2 the respiratory rate range that will used to determine whether the animal should continue on in the study or if it has reached an endpoint.

   Committee Decision: Stipulated
   For: 13 Against: 0 Abstain: 0

6. **Protocol Title:** 2004-38060A Engraftment of human acute myeloid leukemia (AML) cells; Efficacy of BE4- and Cas9-edited CD34+ cells; Efficacy of BE4- and Cas9-edited CD34+ cells; Efficacy of engineered monocytes for cancer immunotherapy; Engraftment of human ovarian tumor cells; Efficacy of CD133 CAR-NK cells; Optimal tumor dose implantation study
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: SA 1: In an attempt to further study the use of human peripheral blood NK or Cord blood NK cells modified by expression of chimeric antigen receptor, we are interested in understanding what modification is most effective for reducing tumor burden. SA2 &SA3:In an attempt to further study the use of mutation reversed CD34+ cells for the correction of genetic disorders and for broadening the application of adoptive immunotherapies. SA4: In an attempt to further study tumor will be injected via subcutaneous injection at a flank of the NSG-SGM3 mice. Engineered monocytes will be intravenously injected into tumor-bearing mice to evaluate anti-tumor activity of the engineered monocytes. SA5: In attempt to further study NK cells modified by gene knockout and/or expression of chimeric antigen receptor, to broaden understanding effects this against diminishing tumor burden with ovarian cancer model. SA6: To determine the in vivo distribution of NK cells, and the therapeutic efficacy of CD133 CAR-NK cells in the context of prostate cancer. SA7 &SA8: To determine in-vivo functionality of engineered T cells created with different viral and non-viral delivery methods. To determine if CISH KO T cells provide better efficacy.

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

   Comment: The description for Specific Aim 5 in the Experiment Design Section indicates that IL-15 will be administered to the mice, but there is not a procedure included on the protocol for administration of IL-15. Please add this procedure.

   Comment: In the response to Cycle 1 comments, justification was provided for the exception to immediate administration of carprofen for post-procedure analgesia following intratibial/calcaneal injections in mice. However, no response was provided to the Cycle 1 comment inquiring whether an injection of buprenorphine or buprenorphine-SR could be given for analgesia either pre or post-procedure. Please consider and respond to this inquiry, and (if applicable) complete the controlled substances section.

   Comment: The specific aims include 2 pilot studies (2 and 7) and 2 follow up studies (4 and 8). Please clarify how the results of the pilot studies inform the follow up studies, and whether there is the possibility that 4 and 8 will not be

done on the basis of the pilot studies.

Comment: To clarify the absence of pain relief justification, is it true that injections within 24 hours hinder effectiveness, but those beyond do not? Is oral analgesia possible?

Committee Decision: Stipulated
For: 13 Against: 0 Abstain: 0

7. **Protocol Title:** 2104-39046A Long-term cardiovascular monitoring in the sheep: effect of renal denervation in hypertension
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This research works to address the mechanism and importance of the neural-cardiovascular-renal interaction in the development and maintenance of hypertension.

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

   Comment: For consistency across the protocol, please adjust in "timeline" section of the experimental design with respect to when the sheep will be sacrificed. It is described that sheep will be sacrificed 4 months after transmitter/DOCA implant, but in the experimental endpoints section of the protocol it is described that animals may be maintained for up to 1 year after the denervation procedure, and in the dietary modification procedure it is described that animals may be on the modified diet for up to a year.

   Committee Decision: Stipulated
   For: 12 Against: 0 Abstain: 0
   Member 1 out

8. **Protocol Title:** 2104-39056A Role of pressure induced renal inflammation in salt-sensitive hypertension
Species &Pain Class:(A,B) Rat
Question the Research Addresses: The studies will characterize the role of inflammation in the development and progression of salt-sensitive hypertension.

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

   Comment: In addition to food restriction for pre-surgical fasting, you are also providing a modified, high salt diet. Please select both food restriction and diet modification. Please update your responses to account for both.

   Comment: At several points in the Experimental Design you state "trained to a bidirectional turntable cage system" but I do not see a procedure describing how training occurs. Is this positive reinforcement training? Are you using food rewards? Please add a procedure to describe what happens during this training.

   Comment: Per IACUC's "Veterinarian Review Analgesia for Laboratory Animals Guidelines" document, abdominal incisions fall under the moderately painful procedure category and the recommendation is to use either an NSAID + Local line block or an NSAID + opiate. Consider SR-Bup + Meloxicam, since that if what you already have listed for other surgeries with abdominal incisions.

   Comment: RAR's website recommends a dose of 1-2mg/kg SQ for Meloxicam in rats, but all of your surgical procedures list a dose of 5mg/kg. Please review and update. Consult with your RAR veterinarian if you have questions or concerns.

   Comment: It is unclear when you intend to use each anesthetic regimen. Do you intend to use Ketamine + Inactin + Isoflurane simultaneously? In your responses to if a rat is "too light" or "too deep", it sounds as though you will just be adjusting the isoflurane. If isoflurane isn't be used, how will you re-dose the Ket + Inactin rats? Will Ketamine + Inactin alone get you 4 hours of anesthesia?

   Comment: Per IACUC's "Veterinarian Review Analgesia for Laboratory Animals Guidelines" document, abdominal incisions fall under the moderately painful procedure category and the recommendation is to use either an NSAID + Local line block or an NSAID + opiate. Consider SR-Bup + Meloxicam, since that if what you already have listed for other surgeries with abdominal incisions.

Comment: Please include a weighing frequency. Pre-op and then weekly post-op seems appropriate. Of course if weight loss is noted (>10%) then rats should be weight more frequently.

Comment: Please provide a frequency for injections (daily, weekly, etc), and maximum number of injections rats receive.

Comment: Note that the Physiology Core has a husbandry SOP (2009-38503), so you can select "yes" to question 1 under the IMHA section.

Committee Decision: Stipulated
For: 13 Against: 0 Abstain: 0

9. **Protocol Title:** 2103-38942A RAS signaling pathways in the maintenance of acute myeloid leukemia stem cells Molecular mechanisms of disease persistence in AML relapse Molecular mechanisms of leukemia stem cell persistence in AML relapse Establishing relationship between MDS and AML Iproteosome inhibitor effects on AML
Species &Pain Class:(A,C) Mice
Question the Research Addresses: We plan to generate mice with genetically engineered forms of chronic and acute leukemia as a consequence of Ras pathway activation and test genetic and pharmacological interventions to prevent or reverse leukemia in these models.

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

Comment: It is mentioned that these new strains of mice are a combination of previous strains bred within the lab. Are there any health affects that have been previously observed in these strains that may be worth mentioning that could affect the quality of life of these animals and would be seen prior to the health affects induced by the injection of the leukemia cells? If so, please add to the Health and Monitoring section.

Comment: 1. Please update the procedure to state how long mice will undergo irradiation. 2. It states mice will be restrained in jigs for irradiation, please elaborate on how the mice will be acclimated to this type of restraint.

Comment: Procedures utilizing oral gavage have all been revised as requested during the veterinary review to state that the volume administered will not exceed 20 mL/kg. While RAR guidelines do provide a range of 1-20 mL/kg for oral gavage in mice, the instruction also advises that administration by oral gavage of more than 5 mL/kg in rodents may cause discomfort and distress because of their inability to vomit. For each of the 5 compounds that you plan to administer by oral gavage, calculations show that the maximum doses that you plan to give should be achievable with a dose volume of 5 mL/kg within the working concentrations that you have provided for each compound. Especially since drug administration by oral gavage for these procedures will be daily for 3-5 weeks, please update procedures with a target administration volume at no more 5 mL/kg, not to exceed 20 ml/kg.

Comment: For the response to question #2 in the Health and Monitoring section, please include the information requested to indicate whether monitoring schedules include weekends and holidays.

Committee Decision: Stipulated
For: 13 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 4)**

1. **Protocol Title:** 1802-35579A Addressing conservation problems using Artificial Intelligence and Statistical Data Integration
Species &Pain Class:(B) Other* (Non-USDA); (B) Other* (Non-USDA)
Question the Research Addresses: How large terrestrial mammals respond to human disturbance (e.g., cattle and poaching) and management actions in the Colombian Orinoquia Region?

Committee Decision: Approved
For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 2001-37801A Development and Translation of an Intracranial Nerve Implant
Species &Pain Class:(B) Nonhuman Primate (Macaques)

Question the Research Addresses: This study will build and evaluate the safety and design needs of a new type of intracranial auditory prosthesis that targets the auditory nerve (auditory nerve implant, ANI).

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

Comment: Please verify that the sedated acoustic brain potential recording procedure will only be performed once per animal. If not, please describe in the experimental design or procedure section itself how frequently the procedure may be performed for a given animal.

Committee Decision: Stipulated
For: 12 Against: 0 Abstain: 0
Member 15 out

3. **Protocol Title:** 1903-36845A MVAP: Training, instrumentation, and qualification of nonhuman primates for sensible enrollment in preclinical trials
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: The primary qualification aspect of this protocol is designed to evaluate individual NHPs planned for use and subsequently prepare them for preclinical studies based on this assessment. Unlike small animal populations which are generally homogeneous phenotypically to a small number of founders, nonhuman primate populations are heterogeneous. This is with the perspective of employing small numbers of highly informative animals in NHP modeling and also ensuring proper comparison in efficacy and safety studies by attempting to eliminate sources of bias e.g. animals that differ considerably in behavior, health status, or condition. Animals are selected using incoming vendor data then fully characterized using behavioral data, veterinary exam data, clinical pathology, immune, and metabolic data obtained during the qualification phase. During basic qualification, all of our animals participate in our NHP training program with the purpose of reinforcing beneficial behaviors and developing basic coping skills. Essentially all training is designed to reframe negative experiences associated with medical management in complex disease modeling. Depending on intended study designation, NHPs may undergo additional preparation (e.g. disease induction, instrumentation, advanced task training). The intended strength of this approach is twofold 1) the ability to stage procedures in a way that minimizes burden on our animals (e.g. cumulative effect/recovery) and 2) support of a 'pool' of ready eligible animals so that animals can complete the program at their own individual pace rather than study-forced timing. In addition, healthy animals in training provide a valuable source of NHP control/reference blood on request, which supports the overall reduction of laboratory use of valuable nonhuman primates by maximizing information obtained per animal through collaboration.

Committee Decision: Approved
For: 13 Against: 0 Abstain: 0

4. **Protocol Title:** 1809-36393A Striatal plasticity in a rodent model of Parkinson's disease with progressive dopamine degeneration
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: First the mitoPark mouse model will be characterized in our hands. We will assess the time course of neurodegeneration and behavioral symptoms associated with degeneration. Second, we will investigate the functional and anatomical adaptations of the principal neuronal type within the striatum, the spiny projection neurons, to determine what adaptations occur prior to the onset of motor symptoms and are thus hypothesized to be homeostatic and what adaptations occur at the onset and after motor symptoms arise and thus hypothesized to be pathological. Another question are trying to answer is we want to know if is if chronic methamphetamine is neurotoxic to and what impact chronic meth use and abstinence/withdrawal has on learning and learned behavior.

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

Comment: For the meth pretreatment group, is meth continued during lever press training? If not, should this be considered an abstinence period? And for this group are pretreatment given before operant sessions (so the only difference is the prior chronic treatment)?

Comment: The limited number of dosages seems insufficient to generate dose/response data. Please justify the limited number of dosages (2) and why those dosages are appropriate for the model. For example, only the 5 mg/kg dosage is mentioned in health and monitoring.

Comment: Under justification for number of animals, I believe there is a copy/paste error. It reads like your adding another 756 animals for the meth experiments. Please clarify.

Committee Decision: Stipulated
For: 13 Against: 0 Abstain: 0

Institutional Animal Care and Use
Committee Minutes
VCRC - 76D
June 14, 2022

Meeting Convened: 12:01 pm	Quorum Requirement: 10
Meeting Adjourned: 1:19pm	Members Present to Vote: 16

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v15.0** of the IACUC Roster

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

1. **Discussion Items**

    1. The committee discussed an SOP submitted by a research group describing their procedures for aseptic surgical technique. The committee requested that language about surgeon hand preparation be edited to include the specific time for scrubbing. The committee accepted the SOP with that change and thanks the group for their work on it.
    2. The committee was updated on a researcher whose privileges to conduct survival surgery in animals have been suspended. A training session has been scheduled and the committee will be updated following that training.
    3. The committee discussed and voted on an updated Policy and Guidelines for the Use and Maintenance of Decapitation Equipment. Language regarding training and proficiency of personnel was added to the Policy and language about specific species that may be euthanized by this method was removed, since the method will need to be approved on individual animal protocols. The revised documents were approved and will be distributed to research labs and posted on the IACUC website for reference.
    4. The committee discussed a situation in which deer mice shipped from a collaborating lab at another institution were found to be unexpectedly pregnant due to a mistake by the shipping institution. The resulting pups were euthanized, and the PI has worked with the collaborator to ensure the correct animals are sent in future. The committee had no further concerns and thanks the PI his prompt communication on this matter.
    5. The committee was updated on the May inspection summary. There were 3 Significant and 17 Minor findings, with one report to OLAW.

2. **IACUC-R1S1(# Protocols: 8)**

1. **IACUC-R1S1 - NEW(# Protocols: 7)**

    1. **Protocol Title:** 2205-39998A Preclinical Evaluation of a Novel Patent Ductus Arteriosus Stent for use in Neonates_SCK
    Species & Pain Class:(B) Sheep (Biomedical)
    Question the Research Addresses: Evaluate the chronic safety and biocompatibility of a novel percutaneously inserted stent into an animal model (neonatal lamb) which is an animal model most representative of the clinical indications for use in terms of anatomy and growth characteristics.

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

    Comment: Can you clarify when in the timeline will the buprenorphine and other pre medications be given from the time the neonate is delivered/cleaned to intubation?

    Comment: Please describe what happens if ewe gives birth before scheduled C-section, what happens to lamb(s) and ewe in that scenario?

    Comment: Can you provide references for where you obtained your dosage for carprofen, do you have literature showing analgesic relief in sheep at this dose? I found review literature describing variable efficacy based on the procedure performed in sheep/lambs, which concerns me that this might not be the most efficacious NSAID out there for sheep. While flunixin has a lot more literature on efficacy and for a wide variety of procedures performed in sheep. Understandably, flunixin has a shorter duration than carprofen so will need more frequent administrations, however, with the lack of literature supporting carprofen use in sheep and how some of ESS procedures can be rather invasive, it is questionable if this is

truly the most effective NSAID for the variety of procedures performed for this group.

Committee Decision: Stipulations must be met
For: 13 Against: 0: Abstain: 0
Members 1, S out

2. **Protocol Title:** 2205-40010A Continued Development of a Percutaneous Heart Valve in the Sheep Model
Species & Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This is protocol is a renewal. The objective of this protocol is the continued evaluation of next generation technology that is undergoing design refinements. This protocol is currently in use for ESS study codes NAPA, TRDT, TKB

Committee Decision: Approved as submitted
For: 14 Against: 0: Abstain: 0
Member 1 out

3. **Protocol Title:** 2205-40008A Rabbit Intramuscular Model for Calcification – SBT
Species & Pain Class:(B) Rabbit
Question the Research Addresses: the rabbit intramuscular model will be used to assess the calcification potential for bioprosthetic tissue that may potentially be used in BHVs.

Committee Decision: Approved as submitted
For: 13 Against: 0: Abstain: 0
Member 1 out

4. **Protocol Title:** 2202-39825A Quantifying heterogeneous impacts of invasive zebra mussels on walleye habitat, food webs, and mercury concentrations
Species & Pain Class:(A,C) Other; (A,C) Other; (A,C) Other
Question the Research Addresses: This project addresses three questions: 1. What are the effects of zebra mussel invasions in Minnesota lakes on walleye recruitment and habitat and on water clarity? 2. How much do young-of-the-year walleye and adult walleye rely on food from lake bottoms vs. open water, in lakes both with and without invasive zebra mussels? 3. How does the presence of invasive zebra mussels affect mercury concentrations in walleye and what drivers might be causing MeHg exposure shifts?

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

Comment: The numbers in the species section do not match the numbers in Table 1 of the document. How many lakes will be sampled in total? The table states the target sample size per lake is between 20-30 samples and 3-5 sites per lake but the total number of lakes to be sampled is missing to make up the numbers noted in the species section. Please update the protocol to clarify the numbers.

Comment: Under Walleye, 3. a. what does "age-0" walleye mean? This is also mentioned in the experimental design.

Comment: An updated version of the AVMA Guidelines on Euthanasia was published in 2020. That reference should be utilized rather than the 2013 document mentioned in this section. Please clarify that the MS-222 will be buffered prior to use.

Comment: Mentions trying this in 2020, please update dates and with any success or failures from 2020 and 2021 that may impact how effective this method will be.

Comment: Please update to AVMA Guidelines on Euthanasia 2020 throughout the protocol

and update "tricaine methanesulfonate" to "buffered tricaine methanesulfonate" (and ensure you are buffering this compound prior to use) per the reference given.

Comment: What is the process by which you would resort to using the short-set gillnetting procedure? Do you wait until late in the season and move to this method out of necessity to obtain adequate numbers? Or after 1 round of seine netting you move to electrofishing and then to short-set gillnetting? Please describe the flow or process for how it will be determined which method to use.

Comment: Under 2, what is CPUE?

Committee Decision: Stipulations must be met
For: 16 Against: 0: Abstain: 0

5. **Protocol Title:** 2204-39917A Investigating Neural and Auditory Effects of Invasive and Noninvasive Neuromodulation
Species & Pain Class:(B) Guinea Pig
Question the Research Addresses: We aim to characterize the effects of a wide range of ultrasound stimulation parameters on the brain and peripheral nerves in addition to modulation in combination with sound and electrical stimulation of several sensory systems.

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

   Comment: Please update the procedure to identify what sound pressure levels are being employed and identify procedures for dealing with noxious stimulus presentations.

   Comment: The protocol refers to oxygen levels being monitored. Is this pulse Ox? Please update the procedure to include what is the acceptable range, and what will be done if values are outside of that range.

   Comment: Please update the procedure to describe recovery procedures and monitoring.

   Comment: Please consider the use of a sterile drape.

   Committee Decision: Stipulations must be met
   For: 16 Against: 0: Abstain: 0

6. **Protocol Title:** 2204-39920A Ffar4 attenuates neuroinflammation in Alzheimer's Disease
Species & Pain Class:(A,B) Mice
Question the Research Addresses: This work will identify how loss of Ffar4 function contributes to AD and potentially identify a target to improve disease outcome. Ffar4 is involved in several of the same pathways that are responsible for neurodegeneration, including inflammation. By targeting this receptor, it might be possible to redirect the immune response, resulting in improved cognitive function.

   Committee Decision: Approved as submitted
   For: 16 Against: 0: Abstain: 0

7. **Protocol Title:** 2106-39189A Renal nerve activity and modulations in hypertensive Yucatan Pigs
Species & Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: This research works to address the mechanism and importance of the neural-cardiovascular-renal interaction in the development and maintenance of hypertension.

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

Comment: As requested during the previous round of review the dose of the salt supplement should be decreased. It remained unchanged in the revised protocol in the 'experimental design' heading where the procedures are listed. (item number 2): "Salt will be added to the feed (90 mEq/kg sodium and 380 mEq/kg potassium) 7-10 days before the DOCA and Transmitter implant procedure."

Comment: DOCA and Telemetry Implant Procedure, terminal surgery (including attachments). I am uncertain why it is necessary to use a paralytic agent to facilitate implantation of the DOCA implant or to perform a laparotomy. Muscle contractions should be transient during the approach (alternatively, for the implantation procedure, the muscle can be gridded along its fibers to enable implant placement.) I think the use of a paralytic agent should be considered as a last resort, and the procedures should be possible to complete without it. Paralytic agents are not used routinely in veterinary surgery for laparotomies and for subcutaneous/intermuscular implantation of devices.

Comment: All procedures where the use of TX is mentioned. The anesthetic regimen describes the use of telazole/xylazine combination and provides the dose as 1-10 mg/kg. This is confusing because I do not know for which constituent you are providing a dose for? Or is that the amount of the 3 drugs combined? (tiletamine, zolazepam and xylzine?). In my opinion, the point of preparing the TX solution is that it is administered by volume afterwards. In general the following dosing is used: administer at 0.05-0.1 ml/kg IV or IM which is equivalent with a combination of 2.5-5 mg/kg tiletamine, 2.5-5 mg/kg zolazepam, and 1-2 mg/kg xylazine. I suggest spelling out this information and provide the dosing in mL/kg for the cocktail. Also, if you prepare the TX solution as you describe (Telazol/Xylazine (TX) Solution 500mg bottle - 100 mg/ml Telazol and 20 mg/ml xylazine.) then in any potential dosing regimen the amount of telazole has to be 5 times the amount of xylazine. That is, dose range of Telazole 1-8mg/kg AND xylazine of 1-3 mg/kg is not possible. (if you want to use 1-3 mg/kg xylazine with this cocktail then the accompanying amount of telazole has to be 5-15mg/kg)

Comment: The experimental design states that the term procedure will take place at 45 +/-15 days after DOCA and transmitter implantation. This is in conflict with the proposed 6 month maintenance of the miniature pigs on the protocol as stated in the experimental endpoints section. It is also mentioned that animals may undergo US exam if there is a clinical need (lethargy/increased respiratory rate). Why is this mentioned here and not in the 'health and monitoring' section? What are you expecting to find during your US? I am surprised by this choice of ancillary diagnostic method. Why not run a bloodwork instead? I imagine the primary complication one can expect is salt toxicity... Please explain the choice of US.

Comment: Term procedure: If the abdomen is approached through the midline then the incision will split the linea alba, therefore the underlying muscle layers cannot be incised individually, in fact no muscle layers are incised at all. Description of the closed- and open-loop electrical block are one and the same except the words "left" and "external" are missing from the closed-loop description. Also, you mention that when time permits the same procedure will be performed on the right kidney. If you are considering to do this, then it has to be described elsewhere including description of the term procedure lasting up to 1+4 (left kidney)+1+4 (right kidney)=10 hours

Comment: The ceftiofur dose used in the protocol is inconsistent. Some places it is 5 mg/kg (procedures, attachment - telemetry replacement table 4; DOCA and telemetry implant - table 4) other places it is listed as 3 mg/kg (attachment - telemetry replacement table 1 ; DOCA and telemetry implant - table 1). Please reconcile this discrepancy.

Comment: Description of the open and closed loop e-block is missing under the subheading "procedures". It describes 1: "DOCA, Transmitter implant, and Modifications to diet and drinking water:" and 2: Acute procedures (including RDN and Sham procedures). Please add this to the protocol. .

Comment: Under the justification for Animal Numbers heading the protocol describes "group sizes of n=36." I am not sure if this is typo, but previously the protocol stated that the number of animals in the RDN and sham groups will be 5 and in the two e-block groups n=10. Please update the protocol to clarify.
Response: The current n=36 is correct, I noticed the error on the first resubmission.

Comment: As other reviewers have stated, please update the text under justification for number of animals. Right now it reads that n = 36 for a pilot study, but really your group sizes are n's of 5 and 10. While it is common to ask for an additional ~10% number animals in case of unexpected adverse outcomes, you're asking for 6 (~16%) additional sheep. If you're expecting a higher mortality rate, please elaborate.

Comment: The protocol states: "Please see attachment entitled "Acute/terminal procedures" for procedural description." There is no attachment that matches the above title. I think you might be referring to the attachment entitled "term procedure FINAL"--please clarify.
Response: Yes we mean Term procedure - final. Clarified

Comment: I think the surgeries "Terminal procedures" and "Unilateral and bilateral Kidney Denervation; Sham procedure" refer to the same interventions thus one of them are redundant. Please clarify.

Comment: I'm not sure I understand how housing sheep individually will allow them to become hypertensive. Is the concern that they aren't eating enough when group housed? Could they be fed separately but still housed together overnight? Or multiple salt licks added to the pen? Perhaps the sentence should be updated to say "sheep could have their intake monitored if the expected rise in blood pressure is not observed and this might result in the need to be temporarily housed alone."? You say that sheep will be a fed a high salt diet and given high salt water for up to 1 yr, but this study is only 40 days. While weight is a good indicator of dehydration, you should also check moistness of the mucus membranes and whether or not their eyes are sunken.

Comment: In response to "How long will animals be maintained after surgery?" you state "Animals will be maintained for maximally for up to 1 year on this protocol....Animals may undergo US examination approximately every month or if there is a clinical need." but based on the Experimental Design it sounds as though though sheep are maintained 30 days post transmitter implant and you do not have ultrasound examination in the Experimental Design section or anywhere else on the protocol.

Comment: Again you state that animals will be maintained up to 1 year on this protocol, which doesn't answer the question on how long animals will be maintained following surgery.

Comment: As per previous reviewer, the Health and Monitoring section needs to be updated. Remember, responses to question 1 should highlight potential health concerns for al procedures on the protocol. Please incorporate your justification for single housing sheep on this protocol in response to question 5.

Comment: Why does your literature search only go until April 2020? Don't you want to know if there are more recent articles available to hep refine your procedure and potentially improve the quality of life for these animals? Please update you search.

Comment: Since ultrasound is not a procedure listed on the protocol, I'm not sure why you

have done an alternative search for this. The same is true for capsaicin -- is this being administered on this protocol? Both of these documents should be removed. Your other literature search documents have the wrong protocol and appear to have search terms for chronic surgeries and thoracic surgical approaches, neither of which are described on this protocol. Please perform an appropriate literature search and update the protocol.

Committee Decision: Stipulations must be met
For: 14 Against: 0: Abstain: 0
Member 1 out

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 1)**
    1. **Protocol Title:** 2101-38763A Adapting high expansion foam for use in American systems for mass depopulation and on-farm culling
    Species & Pain Class:(B,C) Pig (Agricultural); (B,C) Turkey; (B,C) Cow (Agricultural); (B,C) Chicken
    Question the Research Addresses: The objectives of this collaborative work between researchers at the University of Minnesota and international consultants are to use high expansion nitrogen gas-filled foam method for mass depopulation of swine, adapt the method for on-farm euthanasia in American systems, and build acceptance and promote adaption of the technology by performing outreach and education to American stakeholders. A more specific question has been generated based on the turkey results so far; such that activity of poultry within the chamber may influence the generation of the foam and more gradual release of N2 than the previously identified sudden release of nitrogen gas. Hence we need to do a species comparison as most the of the previous work with this method of euthanasia has been done with broiler chickens. The question is: Does normal bird activity in the chamber influence generation of foam and release pattern of nitrogen gas?

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

    Comment: Please include a statement under the Justification for Number of Animals section to account for the proposed 220 chickens.

    Committee Decision: Stipulations must be met
    For: 16 Against: 0: Abstain: 0

Institutional Animal Care and Use Committee Minutes
VCRC - 76D

Meeting Convened: 12:00 PM	Quorum Requirement: 9
Meeting Adjourned: 1:13 PM	Members Present to Vote: 16

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	X	(O, U)

Institutional Veterinarian:

A	X	(M, V)

Correlates to Version **v4.0** 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

1. The committee welcomed new Interim Vice President for Research Dr. J. Michael Oakes.

2. The committee discussed an update from a PI that was permitted to use an Instant Pot for surgical tool sterilization on a trial basis. No infections or other issues have been seen. Autoclave tape has been used as a sterilization indicator, and the committee requests that biological indicators be added going forward. Another request has been received from Duluth, and the committee will require more information before any additional exceptions will be made for other PIs.

3. The committee discussed an update on a self-report involving unapproved imaging. The PI reports that the results from this have not been published or planned for publication. The committee considers the matter closed.

4. The committee reviewed a self-report in which food restriction was conducted for 12 hours without being approved on the protocol. The lab will not conduct this procedure again until an amendment regarding this procedure has been approved. The committee will consider the matter closed once the amendment has been received.

5. The committee discussed the nationwide shortage of pentobarbital and agreed that due to this shortage, pentobarbital-containing solutions may be used for euthanasia for up to three months past the manufacturer's expiration date. These solutions must be inspected for any visible signs of contamination or degradation, and a secondary method or confirmation of death must be performed to verify effective euthanasia. This provision will be reassessed in three months based on the conditions at that time.

IACUC-R1S1(# Protocols: 8)

IACUC-R1S1 - NEW(# Protocols: 8)

1. **Protocol Title:** 2105-39080A Development of a Calcific Model to Evaluate Novel Transcatheter Heart Valve Designs
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This model has the potential to be a better representation of the clinical disease. Additionally it be more beneficial in determining the safety of minimally invasive heart valves during deployment and in life evaluation. In previous work, this model has been shown to effectively mimic the clinical condition of aortic stenosis requiring a TAVR valve in the sheep model, and has demonstrated effectiveness for the chronic evaluation of novel and commercially available TAVR devices. Based on these promising results, we want to continue to create the CAM model for further evaluations of novel and commercially available TAVR devices.

   Committee Decision: Approved
   For: 14 Against: 0 Abstain: 0
   Members 1, 10 out

2. **Protocol Title:** 2105-39099A Assessment of the Impact of unilateral PA stenosis on right ventricular afterload using intracardiac Pressure-Volume loops in a sheep model.
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: Several research studies looking at exercise physiology in children with unilateral PA stenosis suggest a significant improvement in stroke volume response after an intervention, suggesting a role of elevated RV afterload in the hemodynamic alterations amongst these patients (Hiremath et al, Sutton et al). Our goal is to shed more light on the hemodynamic implications of unilateral PA stenosis on the RV afterload.

Committee Decision: Approved
For: 14 Against: 0 Abstain: 0
Members 1, 10 out

3. **Protocol Title:** 2105-39117A Intravenous, allogeneic stem cells for the treatment of induced osteoarthritis in the dog
Species &Pain Class:(B) Dog
Question the Research Addresses: The objective of this research is to identify the influence of treatment (intravenous, allogeneic stem cells or placebo) on limb function and histopathologic disease in dogs with induced stifle OA.

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

   Comment: Please specify the barbiturate to be used for euthanasia.

   Comment: Please add the hydromorphone, tramadol, and the euthanasia drug to the controlled substances page.

   Committee Decision: Stipulated
   For: 16 Against: 0 Abstain: 0

4. **Protocol Title:** 2103-38939A Evaluation of Nocita as an infraorbital nerve block agent in dogs undergoing surgical exodontia from the maxillary quadrants
Species &Pain Class:(B) Dog
Question the Research Addresses: Primary: What is the effectiveness of Nocita for intra-operative pain management when used for infraorbital nerve block versus bupivacaine in dogs undergoing maxillary dental extraction? Secondary: What are the clinical side effects of Nocita when used for infraorbital nerve block?

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

   Comment: The protocol describes wanting to determine potential side effects. In question 1 of this section, the only potential side effect that was listed, was an allergic reaction. Are there any other potential side effects? If so please update the protocol to list what they might be and what is needed to be done, if anything.

   Comment: Please update the client consent form to provide instructions to owner relative to any adverse reactions once the dog is home; also include the expectation that they provide information via email and on the phone regarding any observations.

   Committee Decision: Stipulated
   For: 16 Against: 0 Abstain: 0

5. **Protocol Title:** 2105-39068A LAP: Platform for assessing novel immunosuppressive or tolerogenic strategies using a nonhuman primate liver transplant model
Species &Pain Class:(B) Nonhuman Primate (Macaques); (B) Pig (Biomedical)
Question the Research Addresses: Transplantation saves lives and dramatically improves patient quality of life, however a trade-off occurs because donor organs and cells are not an identical match and require ongoing immunosuppression (medication that prevents the body from attacking foreign tissue), exposing patients to risk of developing serious infections or cancer. This research is designed to evaluate strategies that reduce the toxic side effects of immunosuppression while

protecting the liver graft and/or strategies that train the immune system to think the donor tissue is not foreign, to support successful graft function and survival with no maintenance immunosuppression, this is called immune tolerance. Immune tolerance or novel immunosuppression strategies may allow for the possibility of transplanting organs and tissues between different species.

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

Comment: Please clarify what agents will be used in combination and what determines which agents are used. For example, in a subsequent procedure telazol is mentioned as an alternative to ketamine/mdz. If that applies to all procedures involving sedation, please alter appropriately.

Comment: A group size of 6 is referred to, which presumably applies to both pigs and monkeys, but makes the animal numbers requested unclear. Please update to clarify.

Comment: The functional endpoint criteria for euthanasia is described as serum creatinine >5 mg/dl or blood urea nitrogen >100 mg/dl on two consecutive measurements. However, in the attached detailed protocol and health and monitoring, the functional endpoint criteria is described as total bilirubin >20 or an INR >5 for two consecutive measurements, which I believe is the correct criteria for liver failure. The former may have been an oversight from a previous kidney transplant protocol.

Committee Decision: Stipulated
For: 15 Against: 0 Abstain: 0
Member 16 out

6. **Protocol Title:** 2105-39083A MPSC-Preclinical studies of pluripotent stem cell-derived myogenic progenitors in nonhuman primates
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: Primates have been extensively used in preclinical studies for PSC-based cardiac regeneration, but have yet to be fully explored in the context of skeletal muscle diseases. The fully characterized major histocompatibility (MHC) complex in the Mauritian cynomolgus macaque NHP is remarkably similar to humans. Transplanting iPS cell-derived myogenic progenitors using a clinically relevant technique provides an opportunity to study graft acceptance or rejection in an environment of near-human biological complexity, which addresses a number of aspects related to validity in the evaluation of cell-based therapies.

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

   Comment: Please clarify why three separate blood collection procedures are created. Essentially the same procedures done via vascular access port and small sample volume 1.1 ml, 0.1 ml and 0.5 ml. Why not propose weekly 2ml (or more) blood sampling and use it for different downstream analysis?

   Comment: Please clarify CBC/Chem-single sample vs iStat CBC/CHEM. Are these both included just for flexibility or is there a specific scenario when one would be used vs the other.

   Committee Decision: Stipulated
   For: 15 Against: 0 Abstain: 0
   Member 16 out

7. **Protocol Title:** 2104-39017A Development of anti-strychnine monoclonal antibodies for the treatment of strychnine toxicity
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: One potential treatment option is passive immunization using

monoclonal antibody (mAb) treatment to reverse strychnine-induced convulsions. Using strychnine-based hapten conjugates, mice will be immunized to induce production of strychnine-specific antibodies and B cells, and hybridomas will be generated using splenocytes from immunized mice. In a follow up study, mice would then be exposed to strychnine and once convulsions were induced, either non-specific mAbs or strychnine-specific mAbs would be administered to reverse convulsions. The aim would be to demonstrate that anti-strychnine mAbs can reverse strychnine-induced convulsions.

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

Comment: The experimental design suggests that some animals (10% of total for attrition) might not be used in procedures. Please update the protocol to provide an end point for these animals.

Committee Decision: Stipulated
For: 16 Against: 0 Abstain: 0

8. **Protocol Title:** 2103-38962A Interactions of neural networks activated by pain and Alcohol Use Disorders (AUDs) or itch
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: We will: 1) whether chronic alcohol exposure exacerbates persistent pain; 2) whether pain and itch are processed by distinct or overlapping neural networks.

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

Comment: Please list this procedure under "Dietary and Fluid Modifications" rather than "Behavior" and ensure all questions under this section are fully addressed.

Committee Decision: Stipulated
For: 16 Against: 0 Abstain: 0

June 28, 2022

Institutional Animal Care and Use Committee Minutes

VCRC - 76D

Meeting Convened: 12:03pm	Quorum Requirement: 10
Meeting Adjourned: 2:40pm	Members Present to Vote: 16

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v15.5** 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 Items

1. The committee discussed potential changes to the way IACUC protocols requiring IBC approval are managed. Due to recent incidents in which IACUC investigators using infectious agents in animals were not listed as personnel on a relevant IBC protocol, the committee decided to begin withholding final IACUC approval until IBC approval is confirmed, rather than allowing the PI to affirm that IBC-related work will not commence prior to IBC approval. The IBC section of the IACUC protocol form will be updated to provide more clarity on when IBC approval is required. Specific investigators involved will be contacted to request more information about how this noncompliance occurred and how it will be prevented in future.
2. The committee was updated on the approval of a lab's SOP for surgical practices. There were no further comments.
3. The committee was updated on an investigator whose survival surgery privileges had been suspended by the IACUC. The investigator participated in a training session on aseptic technique. The committee voted to allow the investigator to resume survival surgeries, but requests to be notified when the next surgeries are planned and reminds the investigator that increased post-approval monitoring should be anticipated.
4. The committee discussed an investigator whose use of cats had been suspended by the IACUC. The lab has submitted a new protocol that is limited in both animal numbers and procedures. After extensive review, the new protocol is ready for approval. The committee voted to reinstate the investigator's ability to use cats, in accordance with the new protocol and previously submitted corrective action plan. The committee requires that all anesthetic procedures in cats be supervised by either RAR veterinary staff or VMC anesthesiologists and be scheduled in advance at a mutually agreeable time. The committee will reassess this supervision requirement and the overall success of the lab regularly.
5. The committee discussed a report of an adverse event in which a pig died during preparation for an MRI. The committee was satisfied with the lab's plan to prevent future adverse events, which includes having RAR staff manage anesthesia, and considers the matter closed.
6. The committee discussed a self-report in which errors in drug administration during surgery resulted in the death of five mice. The lab has implemented several changes to prevent a recurrence of these errors, including performing fewer surgeries per day, new checklists and study forms, and retraining of staff on roles and responsibilities. The committee was satisfied with the detailed plan and considers the matter closed.
7. The committee discussed a self-report in which RAR sentinel mouse cages were placed on a rack without access to water, resulting in dehydration and the death of two mice. RAR has planned group meetings and training for all staff to emphasize procedures for ensuring water is provided to all the types of caging in use. The committee considers the matter closed but requests to be kept updated as the planned meetings occur.
8. The committee discussed the Policy and Guidelines for the Use of Photography, Video and Audio Recording of Animals Used in Research and Teaching. It was noted that there is some ambiguity as currently written as to what circumstances require IACUC permission. Updates will be drafted to clarify the requirement that all use of photography or video, including live feed, be described in the IACUC protocol for committee review and approval, and that security measures should also be described.

1. **IACUC-R1S1(# Protocols: 11)**
    1. **IACUC-R1S1 - NEW(# Protocols: 9)**
        1. **Protocol Title:** 2204-39933A Survey of osteoclast genes involved in homeostastis
        Species & Pain Class:(A,B) Mice; (B) Mice
        Question the Research Addresses: We have identified several genes selectively expressed in osteoclasts. We will characterize the role of osteoclast specific genes in bone homeostasis by measuring bone mineral density (BMD) in mice deficient for such genes. Finally, we will study the effects of these mutations on the ability of bone marrow monocytes (BMM) or splenocytes to form osteoclasts ex vivo and resorb bone. Our goal is to establish the role that these genes play in osteoclast differentiation and function, and ultimately in regulating bone mass in vivo.

Committee Decision: Approved as submitted
For: 14 Against: 0 Abstain: 0

2. **Protocol Title:** 2205-40015A Evaluation of a novel coronary bypass graft in the sheep model – XCS
Species & Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: The purpose of this study is to evaluate the experimental graft in a long term animal model. This test article will be implanted and evaluated in a chronic sheep mode to determine the biocompatibility of the material as it is implanted for up to 2 years.

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

   Comment: In the "coronary artery bypass graft surgery" procedure, it is listed that other possible survival surgeries may be at 3 mo, 6mo, 9mo, and 12mo; In the "cardiac catheterization procedure", this same list also includes 1.5 mo., depending on anticipated study endpoint for the animal. Please adjust one of these lists for consistency.

   Committee Decision: Stipulations must be met
   For: 12 Against: 0 Abstain: 0
   Members 1, 11 out

3. **Protocol Title:** 2205-40062A Continued Evaluation of a Novel Tissue Graft in the Sheep Model - XAV renewal
Species & Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: Whether engineered vascular grafts lead to non-thrombogenic surface in small diameter vascular graft applications.

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0
   Members 1, 11 out

4. **Protocol Title:** 2204-39918A Response of the Reproductive Tract to Avian Influenza Virus Infection, In Vivo and In Vitro
Species & Pain Class:(A) Turkey; (A) Turkey
Question the Research Addresses: 1. How the response of the reproductive tract to AIV infection changes at different stages of production? 2. Can we develop reproductive tract organoids as an in vitro model to study the AIV infection?

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

   Comment: Commercial farm sampling (Part A): 1. It is not clear how many farms will participate in the study. From the experimental design, it seems only one farm will be needed because samples will be collected from the same flocks at 3 time points (1st, 2nd, and 3rd outbreaks). However, in the procedure, it is stated “commercial farms”. Please update the protocol to clarify how many commercial farms will be involved in the study, and how many birds will be sampled from each farm. 2. Please update the protocol to define AIV outbreaks (e.g. 10% or 50% of birds infected), and define the 1st, 2nd, or 3rd outbreak (e.g. what are the time intervals between each outbreak). 3. It is not clear how AIV infection will be confirmed, and who will confirm it. 4. Please clarify who will select “infected and non-infected breeder hens” on each farm, the investigators or farm staff? 5. Please clarify whether commercial farms for sample collection have been identified.

   Comment: [redacted] sampling (Part B): 1. Suggest adding the sentence (from Experimental Endpoints) “turkey hens will be housed for up to 2 weeks after arrival on campus. This time period allows adaptation for the turkeys to facilities prior to euthanasia and sample

collection" before "Bird care for campus housing …..". 2. It is not clear which commercial farms turkey birds will come from, whether health status of the commercial farms (e.g. AIV infection history) will be considered, and whether the birds will be guaranteed on [redacted]. Please update the protocol to clarify. 3. How will turkey birds be selected for the study? For instance, will the health status, body weight and age (18 to 34 weeks of age is a wide range) of birds be considered?

Comment: On [redacted]: It would be helpful to indicate what euthanization method will be used.

Comment: On commercial farms: Should the endpoint be the time when the turkey hens are euthanized for sample collection? Why is it stated that 'there is no endpoint'?

Comment: Please include a client consent form for on farm sampling. A template will be sent via email.

Comment: Are the turkeys housed on [redacted] infected or non-infected animals? Are they tested prior to euthanasia or experimentally infected or just naive animals? What information does this group of animals housed at [redacted] add to the study?

Comment: Testing for AIV or confirmation of infection status should be included as a procedure if being performed as part of the study.

Comment: Under 2, it states that commercial farm animals are "under observation of veterinarians assigned to the farms." Are they truly under direct supervision of veterinarians? If not, this statement should be amended to "under observation of the staff/owners of the animals". For daily observations of animals on [redacted] is this by lab staff or is this referring to RAR staff?

Comment: For animals euthanized at the commercial farm, I would include a statement that confirms whichever euthanasia method is used at the farm is in accordance with the 2020 AVMA Guidelines on Euthanasia.

Comment: Are these turkeys going into the food chain? If so, I believe #5 needs to be marked yes.

Comment: Please provide more details on the 30 turkeys used from the [redacted] sampling, similar to as was done for the commercial farm sampling: are these turkeys infected or uninfected animals; do they differ in some way from the farm-sampled animals?

Comment: Please confirm that bird euthanasia by farm staff following "their established euthanasia protocols" will be in accordance with recommended euthanasia guidelines.

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

5. **Protocol Title:** 2206-40139A Feeder mouse colony
Species & Pain Class:(B,C) Mice
Question the Research Addresses: This is not a research protocol - housing feeder mice for live prey training when required at [redacted].

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

Comment: Please provide a secondary method of euthanasia in addition to CO_2 euthanasia

Comment: In this section you mention that there will be cameras monitoring the raptor enclosure when both the mouse and the raptor are in that space. Is this video in some way recorded? How is it stored and what will the video be used for later if it is going to be saved?

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

6. **Protocol Title:** 2203-39855A Ocular surface applications of Descemet's membrane.
Species & Pain Class:(B,C) Rat
Question the Research Addresses: The research will evaluate whether transplantation of cultured limbal stem cell grafts on a Descemet's membrane (a novel culture substrate and carrier) can restore the damaged ocular surface in an rat model of LSCD.

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

Comment: I would consider more frequent daily welfare checks post-operatively within the first two weeks. For example, daily for the first three days after surgery, and then every other day for two weeks, which would include the weekly eye flush as well.

Comment: In the experimental design section, you mention that 5 rats will be used for surgery practice (not included in the study treatment groups). Considering that [redacted] has no previous experience handling laboratory rats and will be trained by RAR, do you think 5 rats will be a sufficient number to perfect the surgical technique?

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

7. **Protocol Title:** 2204-39921A Novel enkephalinase inhibitors, and Guanabenz analogs as analgesics in murine pain model OR Identification of small molecules that regulate endogenous opioid signaling by inhibiting angiotensin converting enzyme
Species & Pain Class:(A,B,C) Mice; (B) Mice
Question the Research Addresses: Can NBEI and E. Guanabenze analogs have an analgesic effect in mice alone or in combination with known pain relievers?

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

Comment: For the Pulse Oximetry procedure, in the event that mice are anesthetized for the procedure, please add to your response to the query about other support agents used during the procedure to indicate whether heat support will be provided to anesthetized animals.

Comment: In this procedure, Acetaminophen, Morphine, and Aspirin are administered to mice as comparative controls for the analgesic agents you are testing. Single dose information is provided for these analgesics in the procedure; please also provide information about the route of administration for each one.

Comment: In the response to Question 2 in the health monitoring section, please add to the description of monitoring by lab staff following the ICV injection procedure to add details about clinical signs to look for and the frequency and duration of health monitoring after this specific procedure.

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

8. **Protocol Title:** 2206-40089A "Test for the involvement of receptor heterodimers in relief of persistent pain using bivalent opioid agonist ligands" "Targeting peripheral GPCRs for relief of persistent pain" "Targeting opioid and alpha-2 adrenergic receptor heterodimers for treatment of chronic pain" DoD proposal 5/27: "Development of non-opioid therapeutics for pain management" OACA FRD #20.28 funded 3/1/21-2/28/22 “Synthesis and characterization of a novel bivalent peripherally directed analgesic”
Species & Pain Class:(A,B,C) Mice; (A) Rat
Question the Research Addresses: What can novel interactions between analgesic receptors contribute to improved analgesic therapies? In particular, how can mu- and delta-opioid receptors (MORs and DORs), α2 adrenergic receptors (α2ARs), and HINT1 proteins be harnessed to improve analgesic therapies?

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

   Comment: Betadine alone is not appropriate aseptic technique for surgery. Please update to 3 alternating scrubs with betadine followed by alcohol.

   Comment: Betadine alone is not appropriate aseptic technique for surgery. Please update to 3 alternating scrubs with betadine followed by alcohol.

   Comment: As this is a procedure that goes into a bone, aseptic preparation of the site prior to injection is needed to help prevent any infection to the site. Hair should be removed, and the site prepared with 3 alternating scrubs or betadine followed by alcohol. I understand this is a model of chronic pain, however, bone penetrance is considered a painful procedure. Will the use of analgesics the day of the procedure affect the study goals as the model is in regards to chronic pain secondary to the tumor, not the injury from the injection? If not, recommend including analgesics just on the day of the injection with an NSAID or opiate. If unable to use an analgesic, please include a statement of scientific justification for why pain medications cannot be used within this procedure.

   Comment: Tetrodotoxin (TTX) is mentioned in this section but I cannot find it anywhere described in the rest of the protocol. Is this toxin being used in this study? If yes, please add a description regarding its use in the experimental design and the procedure section of the protocol.

   Comment: In this section under Aim 2 you mention the following: " We have arranged with RAR to house the 12-16 cages (with wireless hub and laptop computer) [redacted].....". For how long will you house animals in this space?

   Committee Decision: Stipulations must be met
   For: 15 Against: 0 Abstain: 0

9. **Protocol Title:** 2205-40081A Cardioprotective Role of nerol and nerolidol in Cardio-Oncology
Species & Pain Class:(B) Mice
Question the Research Addresses: This research seeks to determine the potential protective effects of nerol and nerolidol against cancer and cancer treatment-induced cardiovascular complications in three mouse models (two models of chemotherapy-induced cardiotoxicity: doxorubicin and carfilzomib and one model of cancer cachexia-induced cardiac dysfunction).

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

   Comment: For Experiment #3, please correct the heading and subsequent text to remove SGLT2 inhibitors and add in nerol or nerolidol.

   Comment: Drug administration: Please correct to reflect the drugs being used in the study, nerol

and nerolidol. The current protocol lists several SGLT2 inhibitors that are not indicated in the other sections of the protocol.

Comment: Please provide a clear protocol for the oral gavage procedure, including the size of the needles, volume administered, and mouse handling.

Comment: What is the purpose of the following procedure, “C26 Colon Cancer Tumor Induction (Second procedure)?” It isn’t clear from the protocol if the C26 cells will be derived from other tumor bearing mice or from cell culture. Please clarify the source of the tumor cells and provide a tumor collection procedure if derived from tumors in other mice.

Comment: Trans-thoracic echocardiography: Please provide and SOP for this procedure, including the use of anesthesia.

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 2)**
    1. **Protocol Title:** 2105-39116A Endovascular Embolic Training Model
    Species & Pain Class:(B) Pig (Biomedical); (B) Dog
    Question the Research Addresses: This is an training course for the instruction of new endovascular surgical neuroradioloists in AVM and aneurysm embolization.

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

    Comment: Why do you foresee the need for two back up animals for each training session when pigs are used, and why are no back up animals requested for dogs?

    Comment: Surgical prep for dogs. Please consider using either F or C for reporting temperature measurements throughout the text.

    Comment: Surgical embolization procedure canine. Please consider providing additional details (at least a brief outline) about the surgical procedure other than: "At this point the training physician will guide trainee to which treatment option is to be performed. "

    Comment: In 'Surgical embolization procedure in canine' you mention that heparin will be administered to maintain ACT at two-times baseline. To achieve this you will need to collect blood form the dogs, however unlike for pigs, there is no blood collection procedure listed for dogs. Please address this discrepancy.

    Comment: In the experimental design you mention that 'A subset of animals will have a CT Angiogram prior to, and on the same day as, the training session.' In the procedures section, there is conflicting information about the per-op CT. You state that: 'After surgery prep (as described in the Procedure Section) and prior to the training session (as described in the Experimental Design Section), animals may have a CT based on the interest of the training session attendees and the availability of the University CT suite.' then you state: 'the CT scan takes place following the surgery, animals will already be intubated and sedated'. Can you clarify when you are intending to perform the CT scan(s)?

    Comment: Please consider adding a brief description of the treatment options anticipated during the surgical embolization procedure.

    Comment: Please add blood collection as a procedure , as blood will be collected during the surgical procedures to monitor ACTs during the cases.

Comment: Please change Acepromazine from .05 - 5mg/Kg to .02 -.05 mg/kg in the paragraph description.

Comment: Are you planning on using the [redacted]

Committee Decision: Stipulations must be met
For: 16 Against: 0 Abstain: 0

2. **Protocol Title:** 2011-38597A Early Development of an Implantable Peripheral Pressure Sensor in an Acute Model
Species & Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: Is is possible to measure pressure in an artery using a subcutaneous ultrasound sensor?

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

Comment: Sensor Testing - Chronic Experiment - For describing the aseptic technique, scrubbing of the operative field is described, but removal of hair is not mentioned (this is true for the sensor replacement procedure as well). I assume you will remove the hair from the operative field before scrubbing. Please clarify. (Indeed, it is mentioned in the attachment, but perhaps it is worth mentioning over here too) - You mention that your goal BP will be 95 +/- 5 mmHg. I think this is a rather ambitious goal assuming you refer to mean arterial pressure. I think aiming for mean arterial pressure >60 mmHg is a more reasonable goal. Does this align with you experience?

Comment: Jacket acclimation and postoperative use - I am a bit concerned how wearing the jackets during the summer months may affect thermoregulation in sheep. Admittedly, I am unfamiliar with these jackets. Are they made of solid or mesh materials? Can you schedule the procedure that the sheep will have to wear the jackets during the colder part of the year (September to May perhaps.) Or perhaps shear the sheep before the jackets are applied? Again, I am uncertain about this issue myself, so please do not hesitate to comment.

Comment: Item 3: Please consider describing the perioperative analgesic regimen (other than ketamine) spelling out drugs/doses/route and duration of administration.

Comment: In this segment, under heading 3, it is stated that animals are monitored at least twice daily. This is in conflict with the statement under heading 2 in health and monitoring where the monitoring frequency is mentioned as DAILY. Could you please reconcile this conflict?

Comment: Please be aware that APIC has a new aseptic technique SOP. The expectation is that this SOP will be followed when procedures are performed in APIC spaces.

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0
Members 1, 11 out

Institutional Animal Care and Use Committee
Minutes
VCRC - 76D

Meeting Convened: 12:00 PM	Quorum Requirement: 9
Meeting Adjourned: 1:17 PM	Members Present to Vote: 12

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	X	(O, U)

Institutional Veterinarian:

3	X	(M, V)

Correlates to Version **v4.0** 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

1. The committee reviewed the May 2021 inspection summary.

2. The committee reviewed a self-report in which animals were left unattended for 30 minutes during recovery from anesthesia. Moving forward, staff will be present in the room during the entire recovery period. The committee considers the matter closed.

3. The committee discussed participation of committee members on inspections. The committee decided the current exemption for not having a second member present for non-USDA housing area inspections will be extended until August 2nd to match University guidelines. IACUC staff will update the assignment of committee members to inspections.

4. The committee discussed a request by a lab on the Duluth campus to use an Instant Pot for surgical instrument sterilization due to decommissioning of the autoclave they currently have access to. The committee requested more information regarding access to another autoclave before making a decision on the request.

5. The committee was updated on communication with a PI using cephalopods in research. There is no update from the PI at this time.

6. The committee was updated on the ongoing discussion of NHP sourcing and potential positive TB test. Additional TB testing has been done, and the lab will continue to monitor the animal while it remains in extended quarantine.

IACUC-R1S1(# Protocols: 12)

IACUC-R1S1 - NEW(# Protocols: 8)

1. **Protocol Title:** 2106-39149A Developing MG53 as a Novel Protein Therapeutic for Acute Lung Injury
   Species &Pain Class:(B) Pig (Biomedical)
   Question the Research Addresses: We wish to establish therapeutic benefits of rhMG53 in a porcine model of ALI. Does the administration of the rhMG53, either aerosolized or IV administered, help preserve the lung function during the early phase of trauma?

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

   Comment: The investigator appears to have omitted an experimental section from the narrative (Objective 2B). About 40 experimental animals are unaccounted for. Please update the Experimental Design to clarify this section.

   Comment: As this appears to be a 3 year renewal, please fill out question E on the Rationale page.

   Committee Decision: Stipulated
   For: 12 Against: 0 Abstain: 0

2. **Protocol Title:** 2105-39105A Porcine Dosing and Imaging Study for Cardiac Adhesions
   Species &Pain Class:(B) Pig (Biomedical)
   Question the Research Addresses: This study will explore the effectiveness of the test therapy in various dosages in preventing adhesions following cardiac surgery, in comparison to clinically available products.

   Committee Decision: Approved
   For: 10 Against: 0 Abstain: 0
   Members 1, 10 out

3. **Protocol Title:** 2105-39128A Evaluation of a novel TAVR valve targeting aortic regurgitation in the sheep

model
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This is evaluation of new technology. This is a novel TAVR design to be used clinically in patients with symptomatic aortic regurgitation without presence of aortic stenosis.

Committee Decision: Approved
For: 10 Against: 0 Abstain: 0
Members 1, 10 out

4. **Protocol Title:** 2104-39043A Immune reconstitution and thymic aging
Species &Pain Class:(A,C) Mice
Question the Research Addresses: Studies will address which cell surface markers, signaling proteins and pathways, cellular metabolic pathways, and cell subsets are important to the pathophysiology of thymic and peripheral reconstitution and also which are amenable to interventional strategies to improve BMT outcome as well as develop leukemia models.

Committee Decision: Approved
For: 11 Against: 0 Abstain: 0
Member 13 out

5. **Protocol Title:** 2105-39108A Agriculture waste: Potential Source of Nutraceuticals for Bio-secure Aquaculture.
Species &Pain Class:(A) Fish (Other)
Question the Research Addresses: What are the metabolic effects of feeding agricultural waste on fish?

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

Comment: Euthanasia by decapitation alone is not acceptable. Unless contraindicated by details of data collection, fish should be anesthetized first (e.g., MS-222) or else euthanized by overdose. Alternatively, if the fish are small enough, rapid chilling followed by decapitation should be acceptable. Decapitation should also be followed by pithing per AVMA guidelines. If anesthesia isn't acceptable given your experimental design, please provide justification why it cannot.

Comment: Blood collection is included in the Procedures, please update the Experimental Design to clarify how blood collection fits into the experiment. Please also include how fish are restrained or anesthetized for this procedure.

Committee Decision: Stipulated
For: 12 Against: 0 Abstain: 0

6. **Protocol Title:** 2101-38763A Adapting high expansion foam for use in American systems for mass depopulation and on-farm culling
Species &Pain Class:(B,C) Pig (Agricultural); (B,C) Turkey; (B,C) Cow (Agricultural)
Question the Research Addresses: The objectives of this collaborative work between researchers at the University of Minnesota and international consultants are to use high expansion nitrogen gas-filled foam method for mass depopulation of swine, adapt the method for on-farm euthanasia in American systems, and build acceptance and promote adaption of the technology by performing outreach and education to American stakeholders.

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

Comment: Thank you for your thoughtful responses and taking time to help educate the reviewers/committee on your proposed experiment. Please update the protocol so that mention of video "recordings" is removed and replaced with some version of "live stream video".

Committee Decision: Stipulated
For: 11 Against: 0 Abstain: 0

Member 3 out

7. **Protocol Title:** 2105-39124A HSV viral vectors to increase peripheral nerve opiate receptors
Species &Pain Class:(B,C) Mice
Question the Research Addresses: We will determine if over-expression of mu-opiate receptors (MORs) in primary afferents increases opiate sensitivity behaviorally after establishment of morphine tolerance.

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

   Comment: In this procedure under "What specific steps will be taken in case any of the measured values are outside acceptable ranges?" you state that if depth of anesthesia in insufficient that you may administer an additional dose of ketamine (1/3 initial dose, IM)", Please correct this to indicate that the ketamine will be given by the IP route. Also please consider adding to this procedure that if anesthesia is too deep, atipamezole (Antisedan) may be given at 1-2 mg/kg SQ or IP to reverse the effect of xylazine to suppress respiration.

   Comment: Your procedure states that "Any animals showing signs of severe discomfort or pain post-surgery or any animals displaying evidence of impaired motor behavior, infection, or substantial weight loss, will be euthanized with an overdose of sodium pentobarbital (Euthasol 100 mg/kg)or ketamine 100mg/kg + decapitation/KCl, isoflurane (5%) + cervical dislocation/decapitation, or carbon dioxide." Please note that ketamine must be co-administered with xylazine for anesthetic effect; ketamine alone should not be used to anestheize mice prior to a physical method of euthanasia.

   Comment: A dose of ketamine 100 mg/kg is listed in this procedure as the anesthetic to use prior to physical method of euthanasia. Ketamine should be co-administered with xylazine for anesthetic effect.

   Comment: Please add euthanasia solution to the list of controlled substances (Pentobarbitol plus active, uncontrolled ingredient should be a choice in the drop-down menu).

   Comment: The procedure for intracranial injections is listed as a class C procedure, yet they are to be conducted under anesthesia (as would be expected). It seems appropriate to be classified as a Class B procedure.

   Comment: The maximum time allowed for the subjects to live following SNI or CFA is listed as up to 120 days. That notable duration appears incongruent with the Experimental Design section where it is indicated that subjects are to receive SNI or CFA 1 week following vector injection and opioid treatment would commence a week following either of those perturbations. Please clarify.

   Comment: In the Experimental Design it is noted that "Mice will be inoculated with one herpes simplex viral vector (see below) by intraplantar or intrathecal injection (~ 10 uL) in awake animals.". However in the Procedures section there is no description of intrathecal injection. Please provide. Additionally, please update the protocol to clarify under what condition would IP or IT injections of HSV vector be provided? When would IP be used and when would IT be used. The rationale for inclusion both routes is not clear.

   Committee Decision: Stipulated
   For: 12 Against: 0 Abstain: 0

8. **Protocol Title:** 2105-39119A Combined Recording and Stimulation in the Fear Circuit for Enhancing Top-Down Fear Regulation "Synchronizing a Fear Regulation Circuit By Temporally Patterned Closed-Loop Neurostimulation"
Species &Pain Class:(B,C) Rat
Question the Research Addresses: In BCI for paralysis, the goal is to detect a patient's intention to move, then deliver electrical stimulation to muscle or spinal cord to cause the desired movement. In the emotional domain, we propose a similar approach: detect the intent/need for emotion regulation by electrical recording, then translate those intentions into stimulation in the limbic circuit. This project takes the first steps towards that by testing a specific closed-loop, emotion-regulation-enhancing design.

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

   Comment: The Species section requests 100 rats in Pain Class C for this protocol. However, the first paragraph of the Experiment Design section describes the project as having 6 groups of 20 rats each (120 rats). The Experiment

Design section describing the intervention specifies 4 groups of 20 rats each (80 rats), and the Attachment describes 3 groups of 20 rats each and one group of 25 animals (85 rats). Please explain and modify the protocol as needed to clarify the total number of animals required for the protocol and provide consistency among sections.

Comment: The description of the surgery was modified in response to Cycle 1 comments to remove the use of glycopyrrolate for respiratory support during the procedure. However, in the section of the procedure under "Please describe intended use if agents will be used in combination". use of the drug is referred to twice more in Options 1 and 2 for Buprenorphine and Buprenorhine-SR. Please remove all references to the drug if it will not be used in the procedure.

Comment: The procedure contains the statement that "This surgery may be done as non-survival, in which case analgesics would not be used." Please provide a brief explanation of the expected circumstances in which this procedure could be performed as non-survival. For example, is this because you expect a certain number of failures during the procedure when the animal would be euthanized, or are a certain number of animals on the protocol used for training, testing, or practice? The need for these non-survival surgeries should be explained in the experiment design section as well.

Comment: It is mentioned that both video recording and behavior tracking will be utilized to determine the effects of the electrical stimulation. Please elaborate on your justification for videoing the animals after electrical stimulation including why video recording is needed in addition to behavior tracking. Also, please describe how long video data will be available to the lab and how those videos will be properly stored or deleted.

Comment: It is mentioned that if animals do not present the preferred behavior or become distress, the "food reward" behavior procedure will be repeated. Please describe the rest time allotted to these animals between the initial behavior test and the repeated session.

Comment: Within this procedure, it is mentioned small screws will be placed on the top of the head to form the base for the head cap followed by "manually tapping in the screw". Please describe more in detail how this will be performed.

Comment: Although it mentions that the animals should be in a mostly healthy condition throughout the study, the health effects listed only cover those post-operatively. The mild shocks and food restriction may also cause health effects and discomfort. Please list the health effects that these procedures could cause and how to alleviate the distress influenced by these procedures.

Committee Decision: Stipulated
For: 12 Against: 0 Abstain: 0

IACUC-R1S1 - AMENDMENT(# Protocols: 4)

1. **Protocol Title:** 2005-38127A Neural mechanisms of choice "Neural basis of reward-based choice" "Repeated cocaine exposure and striatal contributions to cognitive control" "Neural basis of persistence" "Coordinated 3D Marker-less Pose Estimation and Neural Measurements from Freely Moving Rhesus Macaques" "Technology to Realize the Full Potential of UHF MRI" "Center for Neural Circuits in Addiction" NIDA P30 grant "NCS-FO: Neural Correlates of Social States in Macaques" "Traveling Wave Transcranial Alternating Current Stimulation for the Control of Large-Scale Brain Networks" "Neural basis of behavior in freely moving macaques" "Modeling circuit-specific psychiatric deep brain stimulation and its cognitive effects in macaques"
   Species &Pain Class:(B) Nonhuman Primate (Macaques)
   Question the Research Addresses: The general goal of this study is to understand the ways in which the brain's reward and control system drive decision-making, including full body movements

   Committee Decision: Approved
   For: 12 Against: 0 Abstain: 0

2. **Protocol Title:** 2005-38135A Connectivity of motivational brain circuitry Posteromedial cortex circuits in depression and schizophrenia Revealing functional networks and circuits of the posteromedial cortex with anatomical connectivity Academic Investment Research Program ("AIRP"), Center for Neural Circuits in Addiction "Center for Neural Circuits in Addiction" NIDA P30 grant
   Species &Pain Class:(B) Nonhuman Primate (Macaques)
   Question the Research Addresses: We aim to characterize the connections between brain regions involved in motivation. We examine whether particular regions connect to one another, how strongly, and with what organization.

Committee Decision: Approved
For: 12 Against: 0 Abstain: 0

3. **Protocol Title:** 1901-36697A Phase I Study of Midazolam Pharmacokinetics, Pharmacodynamics and Adverse Effect following Intramuscular Injection in Dogs using an Autoinjector Enterprise Diazepam Prodrug/Enzyme Study in Dogs Reliable Seizure Prediction Using Physiologic Signals and Machine Learning Neurophysiologically Based Brain State Tracking &Modulation in Focal Epilepsy Canine Epilepsy: Genetic Variants, Biomarkers, and New Therapies Prodrug/Enzyme Systems for Intranasal Treatment of Seizure Emergencies Allopregnanolone as Initial Status Epilepticus Therapy: Canine Epilepsy Studies Use of Dogs with Naturally-Occurring Epilepsy as a Translational Platform for Evaluating Potential New Therapies for the Treatment of Status Epilepticus
Species &Pain Class:(B) Dog;
Question the Research Addresses: 1. Whether data from an intracranial electroencephalograph EEG (iEEG) can be: 1. used to predict a forthcoming seizure and anti-epileptic drugs (AED) or neurostimulation can be administered prior to the seizure occurring in order to diminish or prevent the seizure. 2. iEEG data used to determine the pharmacodynamic (Pd) effects of new and novel IV and intranasl drugs being developed for seizure emergencies in Epileptic dogs, and pharmacokinetic (pK) studies of the same IV drugs in normal research dogs without and implanted EEG in order to have enough pK data for future clinical trials in dogs and people. 3. iEEG data can be used in conjunction with plasma miRNAs as biomarkers for epileptic seizures. 4. While not specifically indicated the funding for these studies, we are trying to predict seizures before they occur and intervene. Ideally dogs would have 1-2 solitary seizures a month that are stable and not increasing rapidly in frequency that works with both the prediction algorithms and the dogs quality of life. For affected dogs we need at least one seizure every 2 months. There is not lifetime maximum number of seizures and many dogs (and people) can have 1-3 seizures a month that are not becoming frequent and still have a good quality of life. If the seizures regularly become once a week or more often that can be difficult for both the dog and caretakers. Going forward the PI will automatically consult with the RAG veterinarian if seizures are becoming weekly or more often or less often but lasting more than 5 minutes repeatedly for a quality of life discussion and then either the PI or the RAR vet can choose humane euthanasia even if no other IACUC or study protocol criteria have been met.

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

   Comment: It appears that this dog is over 15 years old and has been a research animal in the lab for over 6 years. As the lab has stated, this dog has spontaneously occurring seizures and is on chronic anti-seizure medications. His medical record shows previous episodes of CNS disease (which at the moment seem to have resolved). It appears that there were also previous discussions with RAR veterinarians for one final study to be conducted in spring/summer 2020. But of course it appears that this did not occur. Although it is understandable that some delays occurred in conducting the final study for this research animal due to the COVID-19 pandemic, at this time a more concrete plan for the anticipated use of this dog is needed. A reasonable firm end date by which the animal will be used and then humanely euthanized would be an appropriate course of action. A firm date in the near future is required and the Attending Veterinarian will be following up if one cannot be provided. Although overall apparently healthy, it is obvious that this is a geriatric research patient that is reaching the end stages of his research life. In theory the health of this animal could be declining quickly at any time, and avoiding a situation where humane endpoints are reached quickly would be best. Additionally, once a firm date by which this animal will be used is set, a more close monitoring plan for this animal's health should be developed, so that any decline in health can be quickly detected. I.e. increasing the frequency of physical exam, CBC and chemistry. Please work with the RAR veterinarian to develop this plan.

   Committee Decision: Stipulated
   For: 11 Against: 0 Abstain: 0
   Member 8 out

4. **Protocol Title:** 1911-37623A Addiction connectomics Center for Neural Circuits in Addiction
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: What are the structural changes associated with exposure to addictive drugs? What are the translational mechanisms of addiction that can be gleaned from high-quality connectome data?

   Committee Decision: Approved
   For: 12 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee Minutes

July 12, 2022

VCRC - 76D

Meeting Convened: 12:02pm	Quorum Requirement: 10
Meeting Adjourned: 1:17pm	Members Present to Vote: 12

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v15.5** 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

1. **Discussion Items**
    1. The committee discussed potential updates to the Policy and Guidelines on Photography, Video, and Audio Recording of Animals Used in Research. Draft changes included clarification that use of photo or video for research purposes must be described in the IACUC protocol and the security measures to be taken with both saved and live stream data. Additional edits will be made after consulting policies from other institutions to ensure a comprehensive and robust policy, and the committee will vote on the updated documents at a future meeting.
    2. The committee discussed a minor edit to the Guidelines for Mouse and Rat Survival and Non-Survival Surgery and Post Operative Care. The change clarifies the appropriate use of recovery caging. The committee approved the revised document, which will be posted on the IACUC website.
    3. The committee discussed the process for approval of IACUC protocols that also require Institutional Biosafety Committee (IBC) approval. As discussed at the previous meeting, IACUC approval will now be withheld until any necessary IBC approval has been confirmed. This change in process will be communicated to IACUC investigators via email. Additionally, the IBC section of the IACUC protocol has been updated to clarify requirements. The committee was also updated on two specific situations in which IACUC investigators using infectious agents in animals were not listed as personnel on a relevant IBC protocol. The groups involved have updated their IBC and IACUC protocols appropriately, and the committee considers these matters closed.
    4. The committee was notified of a proposed new IMHA space; discussion of the specifics occurred during review of the protocol amendment requesting the new space (amendment #3 below).

IACUC-R1S1(# Protocols: 8)

1. **IACUC-R1S1 - NEW(# Protocols: 5)**
    1. **Protocol Title:** 2108-39336A Reducing the duration of lameness in dairy cattle by using an autonomous camera-based detection system
    Species & Pain Class:(A) Cow (Agricultural)
    Question the Research Addresses: Can use of Cattle Eye, an autonomous lameness detection software program which scores lameness off of live video feed, combined with prompt and appropriate treatment of lameness cases reduce the duration of lameness by at least 30 days over the use of normal on-farm lameness detection methods coupled with the same treatment protocol? Furthermore, does a reduction in the duration of lameness impact cow production, reproductive performance, and survival to next lactation?

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

    Comment: For the client consent form, please add IACUC contact information to the bottom of the letter. "If you have other concerns or questions about animal welfare you can contact the University's Institutional Animal Care and Use Committee (IACUC) at 612-626-2126. "

    Comment: I'm not for sure the best place to put this information as it somewhat relates to food chain approval but since these are client owned animals and potential treatments may not be known, the food chain question is not applicable in this situation. But it might be helpful to put in the experimental design for lameness treatment, if medications are used, the producer is expected to follow the prescription guidelines for administration and withdrawal times relative to milk or slaughter sales. And to also add this information to the client consent form.

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

    2. **Protocol Title:** 2205-40027A Breeding protocol

Species & Pain Class:(A) Cat; (A) Other
Question the Research Addresses: n/a, i.e., other IACUC protocols require the availability of kittens from postnatal 28 days through postnatal 70 days for various brain imaging projects. While it is known that binocular processing occurs at the back of the brain, in the primary visual cortex, the details of which nerve cells are used is unknown. By using high resolution imaging, research described in other IACUC protocols can ask which cells process information from only one eye (monocular) and which cells combine signals from both eyes and also determine the specific cortical layers in which these cells are located.

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

Comment: Numbers from the "species" section do not match those listed in the Experimental Design Portion, for example, in the Experimental Design portion it states that; "The maximum size of ADULTS in the breeding colony is expected to be 3 males and 6 females" but it lists "10" cats in the species section, not "9". Additionally, if a queen is expected to birth 1-2 litters (each litter consisting of ~2-4 kittens) a year (for an estimated total of ~48 kittens maximum), it is unclear how the number "80" was achieved in the species section. Using the table located at the bottom of the section; 14 litters * 4 kittens per litter = 56 kittens total

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

3. **Protocol Title:** 2205-40054A Murine Hepataprotection from Acetaminophen using novel SIRT inhibitors, guanabenz and Glutathione analogs.
Species & Pain Class:(B,C) Mice
Question the Research Addresses: Can novel glutathione analogs (pGSH) and sirtuin (SIRT) inhibitors confer hepatoprotection from acetaminophen overdose? Is there a hepatoprotective role of guanabanez, pGSH analogs and sirtuin inhibitors in NAFLD/NASH?

   Committee Decision: Approved as submitted
   For: 12 Against: 0 Abstain: 0

4. **Protocol Title:** 2203-39886A Treatment of Preeclampsia Using Cellular Immunotherapy
Species & Pain Class:(A,B) Mice
Question the Research Addresses: Whether immunotherapy is a novel new therapeutic target for preeclampsia and other hypertensive diseases.

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

   Comment: The description of anesthesia states Ket/Xyl may be used, please put that in the anesthesia/sedative chart above.

   Comment: Eye lubricant is required for all rodent surgeries regardless of time to perform, please delete sentence about 5 minutes.

   Comment: You list two different NSAID treatments- Meloxicam and Banamine, it wasn't clear if these were given together or this is just two different options. Please note that two different classes of NSAIDs should not be given concurrently.

   Comment: Due to induction of health conditions during pregnancy please address what happens if female is found dead and pups are born. Or female needs to be euthanized due to dystocia. Are you trying to foster the pups or will all results of dam loss end with pup euthanasia as well?

Comment: Can you expand on the females that may be kept for another pregnancy. Is the osmotic pump removed? Would the pump still be releasing drugs during the second pregnancy?

Comment: Since you take blood pressure and other physiologic measurements are any of those measurements able to be equated to endpoint condition? If so, please include that information in here.

Comment: The health and monitoring section states bup SR may be used and the Osmotic pump section states Ketamine. Please include those drugs here if you will be using them, or delete their mention in the appropriate sections.

Comment: The investigator states that radio-telemetry transmitters will be implanted during the acclimation phase of the study. However, while there is no corresponding procedure description in the Procedures Section, a cuff method for BP measurement was listed instead. Please clarify which BP measuring method will be used.

Comment: The investigator proposes that a cohort of dams be allowed to deliver and then mated a second time to investigate recurring preeclampsia and hypertension. Will these dams be retreated with vasopressin/angiotensin by re-implanting osmotic pumps? If so, the procedure tab needs to be modified to include a 2nd surgical event.

Comment: The investigator proposes that the pups allowed to be delivered will be weaned and then be subjected to a battery of behavioral assessments. Please indicate how these multiple tasks/tests will be scheduled. For example, will all pups undergo each task/test or only a subset? Will there be rest days incorporated into the schedule? How many times will each pup undergo each task/test?

Comment: Regulatory dendritic cells will be used as an immunotherapy treatment. How will these cells be harvested?

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

5. **Protocol Title:** 2206-40127A Prediction of pulse pressure variation and systolic pressure variation on fluid responsiveness in mechanically ventilated isoflurane-anesthetized horses
Species & Pain Class:(B) Horse
Question the Research Addresses: Detecting decreased blood volume is horses is challenging. There is evidence in people and multiple animals that variation in the blood pressure monitoring while a patient is on a ventilator is an excellent predictor of response to additional IV fluids, termed pulse pressure variation (PPV).

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

   Comment: What agent will be used for the local block for catheter placement? Could you include the dose or volume and route of administration?

   Comment: 1)Are the research horses on-site already? Are they covered under another IACUC protocol? If so, please indicate the IACUC protocol number for transfer. 2) Is there a process for donation that indicates the owner/client no longer has responsibility for the animal? I was a bit confused when in the Health and Monitoring section (Question 2), it indicated that if the horse was not suitable for use in the trial, euthanasia would be recommended - Is the recommendation made to the owner? Please clarify.

   Committee Decision: Stipulations must be met

For: 12 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 3)**
    1. **Protocol Title:** 2201-39722A "In vivo MRS and MRI study of metabolism, bioenergetics and function using rodent models" "Advancing simultaneous fMRI-multiphoton imaging technique to study brain function and connectivity across different scales at ultrahigh field" "Development of predictive pharmacodynamic models of ADOR"
    Species & Pain Class:(B) Rat; (B) Mice
    Question the Research Addresses: In this application, we propose to apply the high-field (≥ 9.4T) MRI/MRS to study (i) the hemodynamic, metabolic, electrophysiologic and energetic characteristics and the redox state of normal rodent brains in different brain states; (ii) ischemic brain tissue and therapeutic effect of ADOR using rat model of forebrain (global) ischemia (four-blood-vessel-occlusion (4BVO) model); (iii) glucose metabolism in brain tumor (peripheral gliosarcomas); and (iv) brain function and connectivity across different scales. In addition, we will train lab personnel for the general procedures used in the studies.

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

    Comment: Are the animals anesthetized while restrained for the habituation procedures or are they fully awake (or do they wake up in the restraint device)? How are they restrained in the device - ear posts? Or is the restraint device just a tube it sits in but otherwise can move freely? What damage could occur if the animal is awake and panics trying to escape the device? Just trying to understand the process.

    Comment: Please explicitly define the physiological parameters that would be considered "pseudo-awake"?

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

    2. **Protocol Title:** 2003-37940A Novel Therapies for Sudden Cardiac Death: Mechanisms and Treatments of Diabetic Arrhythmic Risk Mechanisms and treatment of diabetic diastolic dysfunction Diastolic dysfunction and the resolution of inflammation Treatment of cardiac diastolic dysfunction with a mitoTEMPO analog
    Species & Pain Class:(A,B) Mice
    Question the Research Addresses: This proposal aims to explore how diabetes causes those cardiac abnormalities.

    The committee concurs that this protocol will be reviewed via subsequent full committee review once the following stipulations are addressed by the PI:

    Comment: The video procedure states mice are continuously recorded until death--please clarify whether you mean actual death or until IACUC endpoints for euthanasia are met. If you intend to allow mice to progress to death, please update your euthanasia section to indicate you are requesting death as an endpoint and then provide scientific justification for this request.

    Comment: What is the typical timeline for death? Is it a known amount of days, weeks, etc?

    Comment: How will the video/zoom link be secured? Please provide details.

    Comment: Is it possible to use light with reduced intensity and night vision camera for video recording? Continuous light with high intensity may disturb the natural behaviors of the animals and may unnecessarily negatively affect the welfare of the animals.

Committee Decision: Deferral
For: 12 Against: 0 Abstain: 0

3. **Protocol Title:** 2101-38780A XXXX Mouse Protocol Mechanisms and circuitry in mouse models of addiction Academic Investment Research Program ("AIRP"), Center for Neural Circuits in Addiction "Center for Neural Circuits in Addiction" NIDA P30 grant
Species & Pain Class:(B) Mice; (B) Mice
Question the Research Addresses: How do environmental manipulations, particularly drug exposure and subsequent withdrawal, alter the membrane parameters of the nucleus accumbens? How do these drug-induced changes mimic "natural" manipulations, like food restriction, novelty, or stress? What are the long- and short-term consequences for these changes on behavior?

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

   Comment: One HVAC parameter is out of compliance with our IMHA Guidelines. Guidelines state that air exchanges should be between 10-15 air exchanges per hour. Information provided by the lab showed that current air changes per hour in this room are 7.09 (test date 6/13/22). Additionally, it appears this room is negatively pressured. (AIR PRESS. "'W.C. = -0.002). IMHA guidelines state that all housing rooms should be positive in pressure to the corridor [redacted]

   Comment: The phone number for the RAR on call veterinarian needs to be edited to 612-6245440.

   Comment: The lux measurements for the room in question done on 6/13 appear to be for the most part above recommended light levels from the Guide. Per the Guide ", light should be between 130 and 325 lux in the room at cage level".

   Comment: Recommended Air Changes per Hour (ACH) from the guide are 10-15. It appears that the ACH for this room is 7. This is below recommended ACH. Please rectify.

   Comment: Please expand on the scientific rationale for an IMHA. What are your special housing needs that cannot be accomplished in an RAR-managed space? Please note that there are reverse light cycle rooms within RAR vivaria. Regarding controlling for the presence of opposite sex animals, what specific factors do you need to control for (i.e. visual, pheromones, etc.)?

   Comment: Question 6 in the IMHA section references [redacted]. Please clarify whether this is meant to be [redacted] or if this is an additional room being requested.

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

Institutional Animal Care and Use Committee
7/13/21 Minutes
VCRC - 76D

Meeting Convened: 12:00PM	Quorum Requirement: 9
Meeting Adjourned: 1:20PM	Members Present to Vote: 13

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v4.0** 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

1. The committee discussed a preliminary self-report regarding improper genotyping of mice. The committee agreed to table the matter until a formal self-report has been submitted by the lab.
2. The committee discussed a self-report regarding a cage of mice that was dropped during cage change out, resulting in the death of one pup and an injury to another. Animal care staff have been reminded that step stools or ladders are available to help reach the high shelves if needed. The committee considers the matter closed.
3. The committee was updated on reoccurring health issues associated with anesthetic events in a lab using cats. The lab will continue to work closely with RAR on their anesthesia protocol and how to remedy these health issues, and the committee will continue to be updated.
4. The committee discussed the shelf life of drugs in multi-dose vials after initial preparation. A draft policy update will be presented at a future meeting for further discussion.

IACUC-R1S1(# Protocols: 8)

IACUC-R1S1 - NEW(# Protocols: 6)

1. **Protocol Title:** 2106-39202A Topical Hemostat Live Tissue Training Course
   Species &Pain Class:(B) Pig (Biomedical)
   Question the Research Addresses: The objective of the study is to train surgeons and operation room staff on the proper technique for application and use of the Hemoblast Bellows and hemostasis product in a live surgical model.

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

   Comment: I am uncertain why you intend to use a paralytic agent (succinylcholine) for this terminal procedure, please clarify.

   Comment: You mention potential complications associated with ECMO. I did not realize that using ECMO is a part of this protocol. My understanding was that it is limited to the evaluation of the hemoblast bellows and the hemostatic agent. Please update the protocol to clarify,

   Comment: You are listing X-ray as radiations for this protocol. I am not sure what and when you are planning to radiograph. It does not seem to be a part of the research design. Please clarify or remove if this will not be done.

   Comment: Under the heading "description of the surgical procedure" you list 3 potential surgeons including Michelle Dunninng. She is however not listed in the table "Surgeon details".

   Comment: Please update the protocol to specify an estimated number of trainees that are to be trained, and how many animals will be needed per trainee.

   Committee Decision: Stipulations must be met
   For: 12 Against: 0 Abstain:0
   Member 1 out

2. **Protocol Title:** 2106-39159A Role of CFTR in Colorectal Cancer The Role of KCNQ1 in Colorectal Cancer The Role of KCNQ1 in Colorectal Cancer Metastasis The Role of CFTR in Colorectal Cancer

Metastasis Tumor-Infiltrating Eosinophils: A Protective Role in Colorectal Cancer Mechanisms underlying the tumor suppressor role of CFTR in colorectal cancer A novel cancer syndrome in KCNQ1-deficient Syrian Golden hamsters Investigating underlying mechanisms of KCNQ1 tumor suppression using colorectal cancer liver metastasis-derived organoid models The Role of the Intestinal Microbiota in Cancer Pathogenesis and Clinical Care The CFTR gene and colorectal cancer Preventing gastrointestinal cancer in cystic fibrosis Contribution of the oncogenic mutation BRAF V600E to poor prognosis in colorectal cancers expressing low levels of CFTR
Species &Pain Class:(A,B,C) Mice; (A,C) Hamster
Question the Research Addresses: What are the mechanisms underlying the tumor resistance of these genes.

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

Comment: Please fill out the Anesthetic Gases section in the DEHS &OHS tab.

Comment: Please update the procedure to include use of thermal support during animal recovery from anesthesia. Also make sure that all procedures with anesthesia include heat support during recovery.

Comment: Please provide a statement for each genetically modified animal model that there are no strain-specific health concerns, or what health conditions need to be monitored. For example, APC-Min mice used in this study often develop anemia.

Comment: Please consult with IBC regarding whether IBC approval is needed for the use and breeding of genetically modified animals on this protocol. If IBC approval is needed, please include the IBC protocol number on the IBC tab of this protocol.

Comment: Although you mention that the various procedures (surgery, in vivo bioluminescent imaging, tumor induction/metastasis, endoscopy, organoid transplantation, oral gavage, antibiotic conditioning, microbiota engraftment, high fat diets) have been used previously and you wish to retain these procedures within the protocol, please be sure to submit an amendment to update the experimental design section to include the future addition of any of these procedures within your current protocol timeline, or, include these procedures within the experimental design section and label them as "optional" or "future" study.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

3. **Protocol Title:** 2106-39218A Diversity of Leucocytozoon in raptors
Species &Pain Class:(A) Bird (Other); (A) Bird (Other)
Question the Research Addresses: Examine patterns of blood parasitism in raptors based on species, sex, age, seasonality and geography

Committee Decision: Approved as submitted
For: 13 Against: 0 Abstain: 0

4. **Protocol Title:** 2106-39217A Kang Mouse Breeding Protocol
Species &Pain Class:(A) Mice
Question the Research Addresses: This breeding protocol will be used to maintain and expand mouse lines that are needed for research in the laboratory, primarily to examine the genetics and disease mechanisms of muscular dystrophy and other inherited muscle diseases.

Committee Decision: Approved as submitted

For: 13 Against: 0 Abstain: 0

5. **Protocol Title:** 2106-39223A Evaluation of different strategies for pre-weaned dairy calf housing on calf health and performance
Species &Pain Class:(A) Cow (Agricultural)
Question the Research Addresses: Is there a detriment to calf health when housing calves in a modified hutch triplet as compared to individual housing.

   1. Note that the committee discussed and approved the use of video for this study.

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0

6. **Protocol Title:** 2105-39085A Closed-loop neuromodulation for controlling synchrony between brain regions
Species &Pain Class:(B) Rat
Question the Research Addresses: This study will generate pathological synchronization in an animal and test algorithms for optimizing stimulation patterns to maximize efficacy. We will also do histology to map what areas are activated by stimulation.

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

   Comment: Thank you very much for your responses. You are allowed to keep animals [redacted] up to 24 hours after surgery. Please update the protocol to clarify the proposed post-surgical monitoring plan. Animals must be monitored after surgery until fully recovered and ambulatory, but this should take much less than 24 hours, and at that point they can be returned to [redacted] and checked at least once daily, unless there are specific concerns. If you propose monitoring the cages via a camera every 15 minutes, that must be clearly stated in the protocol and scientific justification provided (ie clarify if you will be checking the animals in-person, or via a live feed).

   Comment: Please update your controlled substances protocol with Registrant information.

   Comment: Please update the protocol to describe how the animal is secured stereotaxically, and in particular if there are pressure points for which analgesia might be desireable.

   Comment: Please update the protocol to describe all closing procedures (everything that happens after the microinjection).

   Comment: Both the microinjection and the stimulation procedures state that screw electrodes will be placed symmetrically. Is that true for both procedures, and will there be a total of 4 screw electrodes?

   Comment: Will animals actually be monitored at 15 minute intervals for an entire 24 hour period after surgeries?

   Comment: What doses of bupivicaine will be used for post-operative pain? Please update the Health and Monitoring section to clarify.

   Comment: The behavior section indicates modifications to a number of tests which are not selected (e.g. novelty-induced hypophagia). Please clarify that only rotorod tests will be performed.

   Comment: The rotorod testing is described as two hours prior to surgery #2 and 1 hour after surgery #2, but behavioral procedures describes 3 times daily (900 s or 15 minutes), for up to 3 days. Please clarify.

   Comment: For clarity please include the 5 animals needed for training in the experimental table, and what training is required, and who is giving and receiving the training.

Comment: For sample size justifcation, 3 features of Parkinsonian signal are referred to, but only synchrony and phase relationships are specified. Please clarify and indicate where the 10% success rate estimate comes from.

Comment: Aim 3 refers to termination after anethetized neuromodulation, but Aim 4 refers to behavioral testing after the second surgery. Please clarify that the termination occurs after the second round of behavioral testing.

Comment: There is a reference to a "no treatment folllowed by washout then crossover." How does this apply to electrical neuromodulation? Are sham stimulations being performed on some animals?

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

IACUC-R1S1 - AMENDMENT(# Protocols: 2)

1. **Protocol Title:** 1906-37116A Aligned Nanofibrillar Scaffold Activated with HGF-mmRNA in a Pig Model
   Species &Pain Class:(B) Pig (Biomedical)
   Question the Research Addresses: The central question for this work is to understand if optimizing the biomimetic scaffold in a porcine model can improve skeletal muscle regeneration, vascularization, and function following VML injury.

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

   Comment: It is unclear to me as to why this procedure will need to be recorded. Please provide additional justification as to why you will need to video record this procedure. Will recording the muscle contractions induced by the electrodes be saved for additional assessment later on? If so, please describe how the videos will be safely stored.

   Committee Decision: Stipulations must be met
   For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 1811-36490A Vaccines for fentanyl and its analogs: a strategy to reduce illicit use and overdose
   Species &Pain Class:(B,C) Rat; (A,B) Mice
   Question the Research Addresses: The overall hypothesis is that a vaccine targeting fentanyl and its analogs (either as individual vaccines targeting either fentanyl or its analogs or as a a multivalent vaccine formulation consisting of co-administration of multiple conjugates) will offer selective but also broad protection against the fentanyl-like family. We have employed similar strategies against heroin, oxycodone, and nicotine.

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee 7/26/22 Minutes

VCRC - 76D

Meeting Convened: 12PM	Quorum Requirement: 10
Meeting Adjourned: 1:41PM	Members Present to Vote: 14

Voting:

1	X	Richard Bianco	(Chair - M, S)				
2	X	Erin Dickerson	(Vice Chair - M, S)				
				A	X	Nathan Koewler	(A, V)
				B	X	Whitney McGee	(A, V)
				C		Jessica Felgenhauer	(A, V)
				D		Michelle Reichert	(A, V)
				E	X	Kat Coda	(A, V)
				F	X	Julia Smachlo	(A, V)
				G	X	Jen Hubbard	(A, V)
3		Lynn Impelluso	(M, V)	H		Tim Goldsmith	(A, V)
4		Sally Noll	(M, S)	I	X	Yuzhi Li	(A, S)
	X			J		Paul Lindstrom	(A, U)
				K		Jennifer Borgert	(A, U)
				L	X	Megan McCoy	(A, U)
				M	X	Nima Estharabadi	(A, U)
5		Ilana Cohen	(M, U)	N	X	Kathryn Trautman	(A, U)
6		Henry Wong	(M, S)	O		Georgiy Aslanidi	(A, S)
7		Giuseppe Dell'Anna	(M, V)	P	X	Brenda Kick	(A, V)
8		Dezhi Liao	(M, S)	Q		Markus Meyer	(A, S)
9	X	Ferenc Toth	(M, S)	–			
10	X	[redacted]	(M, St)	R		[redacted]	(A, St)
11	X	Walt Tollison	(M, S)	S		Christin Wright	(A, S)
12		Keith Barker	(M, S)	T	X	Joseph Bump	(A, S)
13		Marilyn Bennett	(M - NA, NS)	U	X	William Sullivan	(A, NA, NS)
14	X	Beverly Norris	(M, S)	V		Craig Flory	(A, S)
15		George Wilcox	(M, S)	W		Carolyn Fairbanks	(A, S)
16		Geoffrey Ghose	(M, S)	X	X	Wensheng Lin	(A, S)
17		[redacted]	(M, St)	Y		[redacted]	(A, St)
18		Laura Stone	(M, S)	Z		Julia Davydova	(A, S)
19	X	Kristin Pilon	(M, U)	AA		Anthony Gray	(A, U)

Non-Voting, Ex-Officio:

i		Sabine Fritz	(O, U)
ii		Jodi Ogilvie	(O, U)
iii	X	Frances Lawrenz	(O, U)

Institutional Veterinarian:

3	*	Lynn Collura Impelluso	(M, V) (*Member A as alternate)

Correlates to Version **v15.5** 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 Items

1. The committee discussed a new Policy and Guidelines on Acclimation and Stabilization of Animals. This policy will require a minimum 72-hour acclimation period (one week preferred) for all animals prior to experimental use. The acclimation period will not apply if only terminal procedures are to be performed. Investigators will be given a two-month period before the new policy goes into effect, in order to plan experiments and submit any requests for exceptions. The committee voted to approve the policy and guidelines as well as the implementation timeline, which will be communicated to investigators via email.
2. The committee was updated on the summary of inspections performed in the month of June. There were four significant and 30 minor findings, with no reports to OLAW.
3. The committee discussed two self-reports from a single lab, both related to inappropriate euthanasia of mice. One mouse was not properly euthanized with CO_2 prior to being placed in the carcass cooler. One mouse pup was left without any adults in a cage with dead pups. In both cases, animal care staff euthanized the affected animal upon discovery. In response to these incidents, the PI will retrain lab staff on proper euthanasia practices. The committee requests that training records for all lab members be submitted for committee review and discussion of any additional steps to be taken.
4. The committee discussed a report of an adverse event, in which mice were found dead or paralyzed following approved tumor cell injection. The lab has worked with their veterinarian to develop a plan, including providing moist food on the cage floor and increasing monitoring by lab staff to twice daily, with prompt euthanasia if neurological signs are seen. The lab will be reminded to ensure that moist food does not develop mold. The committee was satisfied with the lab's plan and considers the matter closed.
5. The committee discussed a self-report in which mice on a restricted food access study were not fed due a miscommunication within the lab. The error was discovered the following morning (less than 24 hours later) and mice were given food immediately. One mouse appeared slow and unbalanced initially but received supplemental fluids and recovered. In response to this incident, the PI has designated lab personnel responsible for checking feeding and communicating with other lab members each day. The committee was satisfied with the lab's corrective action plan and considers the matter closed.
6. The committee discussed an anonymous report that was submitted via the UReport portal regarding mice placed on a rack without lixits by RAR staff, leading to animal deaths. Although the report mentioned dates in July, investigation concluded that this is the same incident that was previously self-reported by RAR (which occurred in May, was reported to the committee in June, and was discussed at the 6.28 FCR meeting) and addressed. The committee did not have any additional comments regarding the reported incident.
7. The committee discussed an issue submitted by an investigator regarding changes to RAR's fasting signage. The investigator reports that the new signage has created confusion, resulting in procedures being cancelled or rescheduled because the animal had not been fasted by RAR as requested by the lab. The lab is concerned that the new RAR fasting signs are unclear as they replaced Start Date and Procedure Date with Fasting Date only. The committee will request more information from RAR as to why the signs were changed and if they can be updated to avoid future confusion.

1. **IACUC-R1S1(# Protocols: 8)**

    1. **IACUC-R1S1 - NEW(# Protocols: 5)**

        1. **Protocol Title:** 2206-40084A A Preclinical Study for the Chronic Evaluation of a Novel Thoracic Graft in the Sheep Model - DTG
        Species &Pain Class:(A,B) Sheep (Biomedical)
        Question the Research Addresses: This protocol will be used to evaluate a novel synthetic graft implanted as its clinically intended use, as a treatment for aortic dissection or aneurysm.

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

            Comment: TAG implant. Minor comment, but I am not sure why you are using an incision on the left side of the neck to access the right carotid artery. I assume this is a typo.

            Comment: TTE. In the procedure description you only mention clinical symptoms as indication for TTE. In the experimental design, it is mentioned that TTE might be performed 7-10d post op then monthly, or in case of clinical signs that can be further evaluated using this methodology. I suggest you just copy and paste the potential indications from the experimental design section for the sake of consistency.

Comment: Terminal procedures. I am not sure why you need a paralytic agent for these procedures. I assume succinylcholine was included accidentally for this procedure (especially considering that the description states: "Succinylcholine will be administered twice, prior to opening the chest and prior to defibrillation while on CPB.") although its use is also described in the attachment... Please clarify or explain. I might very well be wrong here...

Comment: TAG, cardiac cath. and terminal procedures: The anesthetic regimen is not described for either of these procedures. Please consider just mentioning that the same induction and maintenance protocol will be used as described for the MRI and CT procedures or consider referencing the attachments.

Comment: The attachments are very informative but they are not referenced adequately in the main document. Please consider referencing them at the experimental design section (study design attachment) and in the procedures section (surgical procedures attachments).

Comment: This statement is hard to interpret: "We plan on performing cardiac ultrasonography or if clinical symptoms arise. Results from these examinations may necessitate early euthanasia. " I assume you meant to say: In addition to the scheduled cardiac ultrasonographic exams, echocardiograms may also be performed if clinical symptoms are suggestive for cardiac/vascular disorders.

Committee Decision: Stipulations must be met
For: 12 Against: 0 Abstain: 0
Members 1, 11 out

2. **Protocol Title:** 2205-40073A Wild Blueberries as a Novel Therapy to Preserve Cardiovascular Health in Chronic Kidney Disease
Species &Pain Class:(B) Rat
Question the Research Addresses: Recent dietary guidelines for CKD (released in 2020) eased the restriction on FV consumption in CKD, for many proposed benefits, including many recent review articles hypothesizing that bioactive polyphenols in FV may be beneficial in CKD because they combat inflammation and oxidative stress. However, little primary research has been done in this area and none has been done with blueberries; in this study, we will evaluate dietary incorporation of blueberries in a CKD rat model.

   Committee Decision: Approved as submitted
   For: 14 Against: 0 Abstain: 0

3. **Protocol Title:** 2205-40063A Antidepressant Effects of TRH Analogue EEP in Female Rats Assessed with the Forced Swim Test and BDNF Assay
Species &Pain Class:(A) Rat
Question the Research Addresses: Does the thyrotropin-releasing hormone (TRH) analogue EEP (pGLU-GLU-PRO-NH2) have antidepressant effects in female rats measured by immobility in the forced swim test (antidepressant animal model) and by increasing brain-derived neurotrophic factor (BDNF) concentrations in the hippocampus and frontal cortex? The estrous cycle will be assessed to account for any potential differences in immobility or BDNF concentrations that may be related to the estrous cycle.

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

   Comment: In your Experimental Design section, you state, "The animals are run in pairs, with one animal from each cage receiving the experimental compound (EEP), and the cage mate receiving saline." However, the "Overview for IACUC" PDF attachment states that the rats are run "individually" one after the other in cohorts of 3. Please update your Experimental Design to match the PDF document (or vice versa) to show consistent information.

   Comment: In your Health and Monitoring section of the protocol, you have not listed any "anticipated specific study-induced or related adverse health conditions that the animals might experience". Considering that the rats will immediately be put through the forced-swim test following a sub-q injection, I'm wondering if there might be a possible risk of lingering pain from the injection affecting the ability of the animals to tread water?

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

4. **Protocol Title:** 2206-40120A Stem Cells for Treating Acute Stroke; Dose escalation and mechanism of action of exogenic stem cells for treating stroke; Novel highly scalable progenitor cell exosomes for treating stroke
Species &Pain Class:(B) Rat
Question the Research Addresses: We will examine which serum metabolites, cytokines, antibodies, etc, are activated in the area of permanent ischemic stroke and what effect treatment with transplanted stem cells or exosomes derived from these cells has on permanent ischemic occlusions. We will determine where xenogenic exosomes migrate upon induction of ischemic occlusion. Additional studies regarding Poloxamer 188 injection will be done to test the neuroprotective properties of the compound as it relates to ischemic injury. This will be done to gather preliminary data for a further grant.

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

   Comment: If you do not intend to use NSAIDS or Opioids as a form of pain management, please remove them from the sections of the protocol where it outlines their potential use.

   Comment: Please update the descriptive paragraph of the procedure, and the medications list, to include the RAR recommended dose of Ketamine to 40-90mg/kg.

   Comment: Please update the Health and Monitoring section of the protocol to include expected neurological findings, and the specific neurological findings which are of concern and may lead to moribundity.

   Comment: Please ensure that all of your responses to comments in cycle 1 have been integrated into the protocol itself and edits made as needed.

   Committee Decision: Stipulations must be met
   For: 13 Against: 0 Abstain: 0

5. **Protocol Title:** 2207-40197A Fish Use in General Courses and Individual Research Projects
Species &Pain Class:(A,B,C) Fish (Other); (A) Fish (Other); (A) Fish (Other); (A) Fish (Other)
Question the Research Addresses: NA this is a teaching protocol

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 3)**

1. **Protocol Title:** 2003-37962A Development and validation of canine chewing simulator for the study of food-biofilm interaction
Species &Pain Class:(B) Dog; (B) Dog
Question the Research Addresses: Evaluate if a canine chewing dental simulator is able to replicate canine chewing motions and the normal plaque/calculus accumulation in the canine oral cavity and thus be utilized in place of in vivo studies for evaluation of both mechanical and chemical plaque and calculus reducing oral products.

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

   Comment: Experience and training working with dogs needs to be listed for Dr. Chew, including in collection of the samples listed in the protocol and handling of the dogs during sample collection. Alternatively, if the technicians from the Clinical Investigation Center (CIC) will be the ones handling the dogs, this must be clarified on the protocol.

   Comment: Please update the attached Client Consent form to include Dr. Chew as the principal investigator along with her contact information.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 2107-39236A Tracking CD4+ Memory T Cells In Vivo; Protective CD4+ T Cells
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: We are trying to understand how infection causes small naïve CD4+ T cell populations to become large populations of memory cells with diverse functions.

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

Comment: Please update the species section of the protocol with the additional numbers you will be using for the BSL3 studies and include the pain class C animals in this table.

Comment: Mice infected with Mycobacterium tuberculosis will be monitored on a daily basis. Please confirm that animals will be monitored more often when weight loss is close to 25% or if moribund criteria is close to being met.

Comment: Please be sure to add all responses to cycle 1 comments into the body of the protocol

Comment: Please add the housing information for [redacted]. Change the dropdown for housing location to [redacted]", this will generate the [redacted] questions to fill out. If you have questions about how to respond to the [redacted] questions for the [redacted], please contact Thien Sam (samx0002@umn.edu)

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

3. **Protocol Title:** 2104-38973A Physiological-based Pharmacokinetics Approach to Determine the Extent of Drug Exposure of Antiseizure Medications During Pregnancy and Breastfeeding
Status: STIPULATED
Species &Pain Class:(B) Rat; (B) Guinea Pig
Question the Research Addresses: This project focuses anti-epileptic drug clearance and physiological factors determining blood concentrations during pregnancy for both mothers and their unborn children.

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

Comment: This comment also applies to the procedure for catheter retrieval in guinea pigs. The UMN RAR guidelines for anesthesia in guinea pigs advises that "Guinea pigs will store feed in their cheeks and this can lead to airway obstruction. To reduce the amount of material stored in the cheeks the mouth should be gently rinsed with tap water (10-20 ml) prior to induction. The inside of the cheek can also be gently swabbed with a cotton-tipped applicator to remove any remaining material." . Please add this step to both surgical procedures for guinea pigs.

Comment: For both surgical procedures in Rats: " Chronic Indwelling Catheter Implant in Rats" and "Catheter Retrieval in Rats" 1. Please include within the description of the surgery that eye lubrication will be applied to the rat once anesthetized. 2. Dosage of ceftriazone for rat is too high. Recommended dosage for rats is 15 mg/kg SQ (or 0.015 g/kg). Please update. 3. Please include a statement within the question, "What specific steps will be taken in case any of the measured values are outside acceptable ranges?" that if animal is determined to be too light from anesthesia with movements noted, response to toe pinch or increased respiratory rate, an additional 1/3rd the dosage of ketamine will be provided.

Comment: There is mention of a rodent infusion harness that may be used after catheterization, however, no description of this device or housing is included within the protocol. Please include a procedure to describe this and how it will be used, frequency and time rats will be in the harness.

Comment: The health an monitoring section describes, " Infection at the cannulation site is a potential complication; the potential for this complication has been minimized by purchasing animals with cannulas

already in place" within the health an monitoring for guinea pigs. However, as guinea pigs are not purchased cannulated, please remove this statemen.t

Comment: It is described that the catheter will be tunneled and exited out the back of the rat. Please include description of how this site is aseptically prepared/ how sterility is maintained at both the ventral and dorsal surgical sites.

Comment: Sustained-release buprenorphine in guinea pigs is recommended at a dosage of 0.3-0.6 mg/kg through journal articles. Can you please provide the reference for the dosage described in your current protocol (0.5-1 mg/kg)?

Comment: For both surgical procedures in Guinea Pigs: "Chronic Indwelling Catheter Implant in Guinea Pigs" and "Catheter Retrieval in Guinea Pigs" 1. Please include more description of the fasting procedure in the guinea pigs/ the length of time of the fasting. Fasting should only be performed for 2-3 hours. If any of the guinea pigs are in late pregnancy, then no fasting is recommended as this can lead to health issues. Please update 2. Due to guinea pigs storing feed in their cheek pouches, please include a statement that cheek pouches will be examined and feed removed from the cheek pouches prior to surgery via flush with sterile saline and using soaked cotton tip applicator. 3. Please include that eye lubrication will be applied once anesthetized. 4. Dosage listed for ketamine/ xylazine anesthesia should be sufficient for a surgical plane of anesthesia. However, dosage of 87 mg/kg ketamine and 10 mg/kg xylazine also recommended for use for longer surgery to minimize boluses needed. Recommend increasing the range of ketamine to 45-90 mg/kg. 5. Please include a statement within the question, "What specific steps will be taken in case any of the measured values are outside acceptable ranges?" that if animal is determined to be too light from anesthesia with movements noted, response to toe pinch or increased respiratory rate, an additional 1/3rd the dosage of ketamine will be provided. 6. Guinea pigs are prone to develop apnea. Recommend during anesthetic procedure to keep thorax elevated slightly above the abdomen. Please include this within the description of anesthetic monitoring. Also, please include that respiratory rate will be assessed continuously/ closely for signs of apnea and RAR will be called if apnea occurs. 7. Guinea pigs can have muscle spasms as a result of anesthesia and pedal response is not a good indicator of anesthetic depth. Please remove from monitoring. 8. Recovery of guinea pigs should occur on a clean surface/ should not be done on top of corn cob bedding as they can aspirate bedding. Please include a statement that the guinea pigs will not be recovered on corn cob, or corn cob will be covered prior to recovery.

Comment: Ceftriaxone in guinea pigs has been implicated in GI motility issues and gallstone formation with repeated use. Recommend using 10 mg/kg enrofloxacin (Baytril) once SQ.

Comment: For both rats and guinea pigs, please include that for the 3 days following surgery that signs of complications from surgery will be assessed including loss of patency, pallor of the paws (anemia/ blood loss), lethargy, hunched posture.

Comment: 1. Please include a reference regarding pregnancy detection in rats using urine as this is not something I have heard of. Additionally, if urine is going to be collected for this, please include a procedure or information on how urine is going to be collected in the rats. 2. As surgeries are described to be performed within the first trimester, having a better estimate of pregnancy is recommended. Recommend gentle palpation of rats after mating with good records of when rats placed together; fetuses can generally be palpated by gestational day 5-9.

Comment: It is described in the experimental design that urinalysis will be used to confirm pregnancy in the guinea pigs, however, it is not included within the Breeding section. Please include it here and create a procedure to describe how urine is collected from the guinea pigs. 2. As surgeries are described to be performed within the first trimester, having a better estimate of pregnancy is recommended. Recommend gentle palpation of guinea pigs as fetuses can be detected by day 15 of gestation. Ultrasound is the most reliable way to confirm pregnancy in guinea pigs, and is also recommended to help determine a more specific timing of the pregnancy. If have not already, recommended looking at this publication for some useful information: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8482275/

Comment: It is described that the catheter will be tunneled and exited out the back of the guinea pig. Please include description of how this site is aseptically prepared/ how sterility is maintained at both the ventral and dorsal surgical sites.

Comment: There is mention of a rodent infusion harness or guinea pig jacket that may be used after

catheterization, however, no specific descriptions of this device or housing is included within the protocol. Please include a procedure to describe this and how it will be used, frequency and time guinea pigs will be in the harness or jacket or in the specific housing for the infusion. Additionally, if a jacket or harness will be utilized, an acclimation procedure is recommended to ensure the guinea pig will eat/ drink while in the harness or jacket. Please include a description of the acclimation procedure (e.g. how many days, hours, etc the guinea pig will be in the jacket/ harness) prior to the catheterization including what criteria will conclude that the guinea pig is acclimated (e.g. signs eating, drinking, activity, etc) and what criteria wills how that the guinea pig is not acclimated meaning the guinea pig will not be used for the study if they are unable to be acclimated.

Comment: For both catheter procedures, it is difficult to picture what is described in regards to how the catheter will look post surgery/ with the jacket or harness. And how the catheters will be tacked to the skin to minimize chances of them slipping. Please include a paper in the attachments with images or images of what is intended to be used for your studies.

Comment: For both rats and guinea pigs, while it is described in the experimental design section, procedures should be created describing the infusions/ housing systems for the infusions of drugs and expected timeline.

Comment: It is not clear within the protocol how long the guinea pigs or rats are kept after surgery. Within the chronic implant descriptions, it is described that the animals may be kept for up to 90 days, however, if they are pregnant and no births are expected, this timeline is too long. Please clarify the experimental design and timelines. I recommend creating a flow chart to clarify for both rats and guinea pigs describing timelines (breeding/ pregnancy confirmation, surgeries, blood collections, infusions, euthanasia) and including as an attachment to the protocol.

Comment: For both rats and guinea pigs it is eluded to, but never fully described. But what will be involved in catheter patency checks and what is the frequency of these checks? Will catheters also be flushed at a regular frequency as part of the patency checks? This would be recommended at least once weekly to help maintain patency longer.

Comment: For both rats and guinea pigs, please include what clinical signs are monitored as signs of an infection at the catheter site. For example, catheters will be assessed for signs of infection seen as swelling, redness or discharge noted at the catheter site. Systemic infection in the rat (or guinea pig) may be seen as signs of increased respiratory rate or effort, hunched posture, decreased activity/ lethargy. Recommend keeping weekly weights and body conditions scores of the guinea pigs and rats after catheterization to ensure no complications or decreased appetite.

Comment: Please include the dosages, route of administration and name of the barbiturate that will be used for euthanasia (as described in the experimental design) within the euthanasia method section of the protocol. Please also include a statement that the catheter patency will be ensured and catheter flushed prior to euthanasia to ensure catheter is correctly placed.

Comment: There is description of [redacted] being contracted to perform this work, however, it appears this is now [redacted] assisting. Please update information.

Comment: Since the surgeon has experience with rat catheters but the group does not have experience with guinea pigs, please confirm that you will begin with the rat portion of the study before moving up to the guinea pig model.

Comment: Please update to provide the surgeon's experience or proposed training specific to surgery in guinea pigs.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee Minutes

7.27.21

VCRC - 76D

Meeting Convened: 12:01 PM	Quorum Requirement: 9
Meeting Adjourned: 1:15 PM	Members Present to Vote: 11

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v5.0** 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

1. **Discussion Items**

1. The committee discussed the recent AAALAC site visit, on which there were 7 suggestions for improvement and no mandatory findings.
2. The committee was updated on a lab that had a prior adverse event during an anesthetic procedure. Changes to drugs and supportive care were made for the most recent procedure and the animal did well. RAR vets will continue to work with the group to optimize their procedures.
3. The committee was updated on tuberculosis testing results. Serial tests have not increased, so the animal has been released from quarantine. The lab will continue regular testing and will alert RAR to any health concerns.
4. The committee reviewed a self report in which a lab administered an antibiotic at the wrong concentration. The lab proposed updating their IACUC protocol to state that the drug would be acquired from RAR at a ready to use concentration, and updating their surgery form to include the concentration. The committee informed the lab that they cannot rely on RAR to perform dilution for them, and instead need to train lab staff to check the concentration and dilute as needed. The committee will continue to be updated on this matter.
5. The committee reviewed a self report in which burr hole procedures were performed at a time interval closer than approved in the protocol. The lab has updated their SOPs and retrained staff to ensure that the approved timing is adhered to. The committee considers the matter closed.
6. The committee reviewed a self report in which breeding and DSS colitis procedures were carried out on the same animals without approval to combine these procedures. The lab has submitted an amendment to request permission to perform the procedures in the same animals and will not do so unless approved. The committee considers the matter closed.

1.

1. **IACUC-R1S1(# Protocols: 9)**

1. **IACUC-R1S1 - NEW(# Protocols: 9)**

1. **Protocol Title:** 2106-39201A A Preclinical Feasibility Study to Evaluate Novel Mitral Valve in the Sheep Model.
   Species &Pain Class:(B) Sheep (Biomedical)
   Question the Research Addresses: Animals will be used to evaluate the biocompatibility, functionality, durability, and safety of a developmental heart valve.

   Committee Decision: Approved as submitted
   For: 11 Against: 0 Abstain: 0

2. **Protocol Title:** 2106-39205A Cerebral circulation mapping in the sheep model
   Species &Pain Class:(B) Sheep (Biomedical)
   Question the Research Addresses: This study aims to map the cerebral vascular anatomy of the sheep brain using the latest in clinical imaging, which may include computed tomography (CT), magnetic resonance imaging (MRI), transcranial Doppler ultrasound, and fluoroscopy.

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

   Comment: Since this is non-funded research and has not undergone peer review, what type of vascular mapping has already been done if “there are numerous publications with this work done in sheep”. Do none of the 38 papers have adequate vascular mapping or are there specific vessels you are interested in?

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

3. **Protocol Title:** 2008-38367A RF Heating in MRI Including "Safe Magnetic Resonance Imaging of Patients with Deep Brain Stimulation Systems"

Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: How is RF energy deposited? What are the physiologic outcomes of the RF energy deposition?

Committee Decision: Approved as submitted
For: 11 Against: 0 Abstain: 0

4. **Protocol Title:** 2105-39098A Neurobiology of Aggression Escalation; Neurobiology of Female Aggression
Species &Pain Class:(A,B) Hamster
Question the Research Addresses: The research will pursue our novel findings that specific biochemical pathways in the nucleus accumbens (a region involved in motivated behaviors) change with aggressive experience. Further we propose that these long term biochemical changes translate into structural and electrophysiological changes in nerve cells to mediate escalated aggression, even without further aggressive interactions.

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

   Comment: Please update the protocol to include the purpose of castration in male hamsters.

   Comment: There is a Procedure tab for ovariectomy of female hamsters but there is no mention of that procedure in the Experimental Design. Please either update the Experimental Design to include where this procedure fits in, or remove the procedure if it will not be done.

   Comment: A total of 1158 hamsters are requested in the Species Table but only 360 experimental animals are described in the Experimental Design. Please clarify.

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

5. **Protocol Title:** 2106-39224A Umbrella Protocol for the North Central Region Sustainable Agriculture Research and Education (NCRSARE) Projects
Species &Pain Class:(A) Cow (Agricultural); (A) Pig (Agricultural); (A) Chicken; (A) Fish (Other); (A) Sheep (Agricultural); (A) Goat; (A) Rabbit; (A) Horse
Question the Research Addresses: The mission of the NCR-SARE is to strengthen communities, increase farmer/rancher profitability, and improve the environment by supporting research and education.

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

   Comment: This umbrella protocol does not provide sufficient description of procedures that would be performed under the protocol. Please either update this protocol to include more specific descriptions of procedures, or have each investigator apply separately for IACUC approval.

   Comment: Please clarify whether projects in the Farmer Rancher and Youth Ed categories were submitted to the IACUC for review/approval. Please provide protocol number(s) if so, or clarify why not.

   Committee Decision: Deferred
   For: 11 Against: 0 Abstain: 0

6. **Protocol Title:** 2104-39016A Control of cryptococcal infection through manipulation of the host immune response. Impact of Cryptococcus titan cells on pathogenesis
Species &Pain Class:(B,C) Mice
Question the Research Addresses: The specific questions we will be addressing with the animal studies on this protocol are 1) Which T-cell subsets prevent, control, or exacerbate cryptococcal infections, and 2) How do morphological alterations by Cryptococcus (ie titan cell production) affect T-cell priming and function, and 3) How macrophage trafficking and polarization in the lungs controls Cryptococcal infection. Our preliminary studies show that the presence of Th1 cells is correlated with

increased prevalence of macrophages and dendritic cells. Infections with strains that cause lethal disease exhibit increased Th2 and Treg production that is correlated with loss of functional Th1 cells and increased accumulation of eosinophils. The questions posed above aim to determine the role of each of the cell types in control of the infection vs. development of disease, and the role of cryptococcal titan cell production in altering the T-cell response.

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

Comment: Thank you for adding the anesthetic protocol to this procedure. Please also include in the procedure the additional detail needed to address these additional considerations from the U of MN IACUC Guideline for Rodent Tail Biospy. "The tail must be disinfected with alcohol prior to snipping. (Do not use iodine solutions as they may interfere with DNA analysis). Use clean gloves and a sterile sharp scalpel or razor blade. Make one clean cut through the tail. Control bleeding with direct pressure. Observe the mouse in the cage after releasing to assure hemostasis. It may be necessary to cauterize the tail with styptic powder or silver nitrate. The presence of blood in the cage may increase aggression among cagemates."

Comment: Thank you for updating this procedure with specifications for injection volume. While the vehicle for hDT was identified in your responce to comments, please also edit the procedure to include this information and any other steps you are taking to ensure the sterility of the solution which is injected by the IP route.

Comment: The procedure for Tamoxifen Gavage indicates that you plan to give the drug in a volume of 250 uL. Administration of gavage volumes greater than 5 ml/kg may cause distress in species that are unable to vomit. Please either limit the dose volume to 5 mL/kg or justify why it is necessary to exceed that volume in this species.

Comment: The Attachment provides a very detailed explanation for the number of animals required for the experiments on this protocol and I appreciated that it was easy to follow for review purposes. There was one discrepancy between the Attachment where 4134 mice are enumerated to be bred for experiments and the Species section, which requests 4244 mice to be bred for experiments. Please reconcile.

Comment: This procedure states that 19 strains of mice will be bred for this protocol, requiring 65 breeder pairs and 1497 offspring for a total of 1562 mice. Please reconcile or explain why this differs from the number of mice in the Species section which are requested to be bred for this protocol and update the procedure accordingly.

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

7. **Protocol Title:** 2107-39247A In vivo Reporters of Mycobacterium tuberculosis ESX-5 Secretion
Species &Pain Class:(A,C) Mice
Question the Research Addresses: The research will determine when, in what cell types and in what tissue contexts M. tuberculosis induces ESX-5 expression during infection.

   Committee Decision: Approved as submitted
   For: 11 Against: 0 Abstain: 0

8. **Protocol Title:** 2106-39156A Preclinical Cell-based Approaches to Novel Therapies of Pediatric Disorders (epidermolysis bullosa protocol)
Species &Pain Class:(A,B,C) Mice; (A,C) Rat
Question the Research Addresses: Can we define and test novel cellular therapeutics to ameliorate tragic genetic disorders like EB of childhood?

   Committee Decision: Approved as submitted
   For: 11 Against: 0 Abstain: 0

9. **Protocol Title:** 2106-39176A Psychosocial Stress Exacerbates Doxorubicin-induced Cardiovascular Aging
Species &Pain Class:(B,C) Mice
Question the Research Addresses: This research seeks to determine what are the mechanisms of juvenile doxorubicin-induced cardiotoxicity, identify how other cardiovascular risk factors can exacerbate doxorubicin-induced cardiotoxicity, and test potential therapeutic interventions.

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

Comment: In the Rationale for Species Selection, there remains a statement to say that Galectin-3 KO mice will be produced in-house. I see that there is no longer a breeding procedure on the protocol and that the number of mice produced in house has been changed to 0. Please delete this statement if it is no longer applicable (or restore elements to the protocol to support the use of these mice if you still need them).

Comment: Several experiments describe the use of injections for drug administration, but the route of administration is not specified (IP, IV, IM, or SC). Please specify the route of administration for injections. This information could be included in either the Experiment Design section or in the Procedure for Drug Administration; updating in both places is preferred for clarity.

Comment: Please add a procedure for Administration of Biological Materials. This is a companion procedure for your Tumor Induction procedure; one describes the method of tumor implant and the other describes the tumor cell line and its history of rodent pathogen screning for use in [redacted] facilities.

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

Institutional Animal Care and Use Committee Minutes

VCRC - 76D

Meeting Convened: 12:00 PM	Quorum Requirement: 9
Meeting Adjourned: 1:40 PM	Members Present to Vote: 12

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v6.5** 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 Items

1. The committee voted unanimously (12-0) to suspend all animal work by a lab that has had ongoing and serious issues with animal welfare, effective immediately. The suspension will remain in place until the lab develops a strong corrective plan that is approved by the committee.
2. The committee was updated on the July inspection summary.
3. The committee discussed a request by an investigator to continue using an Instant Pot for instrument sterilization long term. The Chair will discuss other options with the PI, as the committee does not consider this a permanent solution.
4. The committee discussed an investigator's responses to questions raised about a recent amendment on a protocol for which no more animals are available to order. The PI will be asked to clarify whether more animals will be requested and reminded that if there are no plans for more animals the amendment is not needed.
5. The committee discussed an adverse event report in which surgical complications led to the death of one animal and early euthanasia of another. The committee was satisfied with the lab's actions and considers the matter closed.
6. The committee was updated on a recent critical citation from the USDA related to delayed reporting of animal mortality in Duluth. RAR will work with Duluth as well as [redacted] and [redacted] to outline additional veterinary SOPs, which will include communication guidelines, and ensure they are followed.
7. The committee was presented with a request for an exception to the *Guide* to allow use of the manufacturer's expiration (9 months) vs the current 6 month expiration date for animal feed. The committee unanimously voted to allow the exception.
8. The committee was updated on the RAR staffing shortage. The situation is considered critical and animal welfare may be impacted soon.
    a. It was noted that messaging to investigators on this matter came from the IACUC email. It was discussed that further messages on this matter should come from OVPR or RAR emails, unless it has been discussed by the IACUC committee in advance.

IACUC-R1S1(# Protocols: 10)

IACUC-R1S1 - NEW(# Protocols: 7)

1. **Protocol Title:** 2106-39174A Contribution of endothelial Jak2V617F expression to thrombosis
   Species &Pain Class:(B,C) Mice
   Question the Research Addresses: These studies will identify disease targets and evaluate compounds in pre-clinical studies to determine their efficacy in mouse models of myeloproliferative neoplasma

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

   Comment: The post-op care for this procedure indicates that the animals will be studied for three days post-implantation, whereas your experimental design indicates that animals will be challenged and measured on the same day as implantation. Please reconcile.

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

2. **Protocol Title:** 2105-39130A Field Methods in Research and Conservation of Vertebrate Populations
   Species &Pain Class:(A) Other* (Non-USDA); (A) Other* (Non-USDA); (A) Other* (Non-USDA); (B,C) Other* (Non-USDA); (A) Other* (Non-USDA); (A) Other* (Non-USDA); (A) Other* (Non-USDA); (A,B) Other* (Non-USDA); (B) Other* (Non-USDA); (A) Bird (Other); (A) Fish (Other); (B,C) Fish (Other)
   Question the Research Addresses: How do wildlife and fish populations change through time, and what

patterns of resources are affecting space use by individual species?

Committee Decision: Approved
For: 11 Against: 0 Abstain: 0

3. **Protocol Title:** 2106-39224A Umbrella Protocol for the North Central Region Sustainable Agriculture Research and Education (NCRSARE) Projects
Species &Pain Class:(A) Cow (Agricultural); (A) Pig (Agricultural); (A) Chicken; (A) Fish (Other); (A) Sheep (Agricultural); (A) Goat; (A) Rabbit; (A) Horse
Question the Research Addresses: The mission of the NCR-SARE is to strengthen communities, increase farmer/rancher profitability, and improve the environment by supporting research and education.

   The committee tables review of this protocol until OVPR legal counsel can review this process and details on how other institutions address these types of submissions can be found

4. **Protocol Title:** 2106-39147A Housing SOP for [redacted]
Species &Pain Class:(A) Mice
Question the Research Addresses: N/A

   Committee Decision: Approved
   For: 11 Against: 0 Abstain: 0

5. **Protocol Title:** 2106-39151A THE UTILITY OF WAVEFORM COAGULATION TESTING FOR PREDICTING PROGNOSIS IN FREE-RAGING BIRDS OF PREY, USING THE TURBIDIMETRIC ACL-TOP CTS 300 COAGULATION ANALYZER
Species &Pain Class:(A) Bird (Other)
Question the Research Addresses: Are abnormal coagulation tests useful in determining prognosis in raptors as they are in mammals?

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

   Comment: A total of 50 raptors will be enrolled in the study and wil be a combination of Bald Eagles, Red Tailed Hawks and Great Horned Owls. Will there be a minimum number for each specific species or will the investigators just use the first 50 birds regardless of species? Please update the protocol to include this information.

   Comment: Please update the protocol to provide a brief explanation as to why birds may be presented to the [redacted].

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

6. **Protocol Title:** 2106-39160A Improving safety profile of flexible bronchoscopy: Novel device to allow intermittent oxygen insufflation
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: This project is a proof of concept / feasibility study of an innovative bronchoscopy device on a swine model. The overarching goals of the study include testing the safety of the device, efficacy, ease of use, and visual field.

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

Comment: For clarification: In the intubated animal, the protocol mentions recovering oxygen saturations from below 70% by using the oxygenation mode on the bronchoscope, and increasing the FiO2 on the ventilator. In the non-intubated procedure, after the animal desaturates below 70%, which methods of oxygen delivery are performed to recover oxygen saturations? Ie. In the non-intubated animals, are the animals delivered oxygen only through the bronchoscope 'oxygenation' mode during saturation, or are they provided supplemental oxygen through a mask?

Comment: Please update the doses in the "Description of the Surgical Procedure" to reflect the recent dose changes of the Anesthetic and Analgesic agents listed for the procedure. For example, Telazol is still listed at 2-8 mg/kg in the description of the surgical procedure, but has been changed to 2-7 mg/kg in the list of agents. (Also Xylazine, Buprenorphine, Vecuronium)

Comment: Please update the doses in the "Description of the Surgical Procedure" to reflect the recent dose changes of the Anesthetic and Analgesic agents listed for the procedure (Telazol and Xylazine)

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

7. **Protocol Title:** 2106-39235A Procedural Assessment of the ARIA CV Device
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This is a training course for the instruction of a new device to treat symptoms of pulmonary arterial hypertension and to evaluate how the effectiveness of the new device.

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

Comment: It appears that the researchers are trying to accomplish both training of physicians/field personnel on the use of the test article as well as data collection to evaluate its effectiveness. Due to this the experimental design section should be expanded to include details of the training as well as the data collection with a clear time line. For the training portion of the study more details are needed. For example, state how many clinicians will be trained per each sheep, how many attempts will each clinician have a placing the device, define what is meant by "multiple times" when it is mentioned in regards to the device placement, etc. For the data collection portion more details about how the data is collected is needed. For example, what kind of data is being collected and how exactly is being collected? will the data collection occur at the same time as the training of a clinician on the device use? If yes, how will quality of data collection be ensured?

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

IACUC-R1S1 - AMENDMENT(# Protocols: 3)

1. **Protocol Title:** 1912-37667A T Cell Responses to Intestinal Protein; Vaccination to reverse established CD8 T cell tolerance to melanoma; Reversing CD8 T cell tolerance in vivo
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: We will determine how immune cell (T cell) differentiation, migration, and maintenance is affected in animals with cancer, chronic infection or in animals bearing a known self-antigen. We will also test how the T cells induced function can be better through vaccination. We also study how the intestinal environment influences the development of pathogenic or tolerant immune cells. Another study will model how fertility is affected in females with IBD.

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

Comment: How is the breeding performance/infertility being assessed/monitored in the animals that are on DSS water and allowed to breed? There is no explanation in the experimental design of this additional experiment and how it will be conducted. Please update the protocol to expand on this. In the procedure section for "breeding mice with colitis" you mentioned that the offspring will be measured and weighed and then euthanized at 3 weeks of age. What exactly is being measured? How often? Will litter size be tracked? Or number of litters produced by a female during a certain time period? Please update the protocol to include this information. Is this a new model or is this an established model of infertility? If this is a new model, then is this study that is being added with the amendment a pilot?

Comment: It appears that 40 animals are being added with this amendment. Please clarify how this number was determined.

Comment: Please edit the Experimental Design to reflect the addition of the infertility studies.

Comment: In the description of the infertility/DSS procedure, the protocol states that the pregnant animals will be allowed to go to term and deliver pups. The pups will be measured and weighed and then kept for up to 3 weeks. Please update the protocol to clarify how many times and when the pups will be measured and weighed. In addition, if pups are measured and weighed prior to the 3 weeks, what is the reason for keeping them that long?

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

2. **Protocol Title:** 1812-36590A Mononuclear Phagocytes in inflammatory disease
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: What mechanisms are utilized by mononuclear phagocytes (myeloid cells, including macrophage, dendritic cell, and monocyte) to promote inflammation associated with systemic and chronic inflammatory diseases, specifically in cardiovascular disease/atherosclerosis and diseases that are directly linked such as obesity and diabetes?

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

Comment: Experiments were added to the experiment design section in the amendment which require more than 500 additional mice, but there was no corresponding revision of the Species section to increase the number of total mice required or to change the number of mice for each Pain Class. Please update the Species section accordingly.

Comment: Thank you for revising the ketamine and xyalzine dose information. Please consider using ranges for the drug dosages as requested in the first cycle of review (80-120 mg/kg for Ketamine rather than 100 mg/kg, and for Xylazine 5-10 mg/kg rather than 10 mg/kg). This will allow you some flexibility which might be helpful if the level of anesthesia you are acheiving is too deep or too light. Particularly for the xylazine, a dose at the high end could potentially cause respriatory depression that could cause you to lose mice during the procedure. You can also add to the protocol a reversal agent for xylazine if the mice stop breathing. Atipamezole (Antisedan) at 1-2 mg/kg can be given SQ or IP to reverse the effects of xylazine. This can be added to the procedure in the section for "other support agents used" or in the section about how you will respond if monitored parameters are out of range. This comment would apply to the Surgery for the in vivo imaging as well.

Comment: The Experiment Design section refers in experiment 2A to the administration of depleting Anti-CCR2 antibody or chlodronate liposomes to deplete circulating monocytes, but I could not find a corresponding procedure which included these. Likewise, experiments 2B and 3A refer to administration of diptheria toxin. Please add procedures to include administration of these materials to the mice, or

clarify which procedure included the instruction.

Comment: The Health and Monitoring section refers to daily monitoring performed by RAR staff as a response to how pain and distress will be monitored. Please be advised that unless you have arranged for extra technical services from RAR staff, this daily monitoring does not include opening any of the cages. Cages of mice which need daily attention to any clinical observations should have increased frequency of monitoring by lab staff.

Comment: I could not find any mention of the cold stress procedure in the experimental design. Please update this to reflect which mice will be exposed to this cold stress and what the determinant for the length of exposure to the cold will be.

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

3. **Protocol Title:** 1907-37192A Chemoprevention of Skin Cancer Program Project Developing new ornithine decarboxylase inhibitors to prevent skin and colon cancer with Prevention of solar UV-induced skin cancer by targeting LTA4H
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: The overall goal is to investigate the role of solar (i.e., sunlight) ultraviolet (UV) irradiation-induced signal transduction pathways in skin carcinogenesis and as targets for chemoprevention of skin cancer. This proposal is aimed toward investigating the role of a variety of proteins known to play a critical role in solar ultraviolet (solar UV)-induced skin carcinogenesis and to establish the importance of each of these proteins as a target for chemoprevention of skin cancer. We have two goals: 1) To determine the role of specific proteins in solar UV-induced skin carcinogenesis by using the respective knockout mice; 2) To study the chemopreventive effect of newly discovered inhibitors of cancer-associated proteins in a solar UV-induced skin carcinogenesis mouse model.

Committee Decision: Approved
For: 11 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee
8/10/21 Minutes
VCRC - 76D

Meeting Convened: 12:00pm	Quorum Requirement: 9
Meeting Adjourned: 1:55pm	Members Present to Vote: 12

Voting Members			Alternates		
1	X	(Chair - M, S)			
2		(M, V)	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)
3		(M, S)	I	X	(A, S)
4		(A, U)	J		(A, U)
			K		(A, U)
			L	X	(A, U)
			M		(A, U)
5		(M, S)	N	X	(A, S)
6	X	(M, V)	O		(A, S)
7	X	(M, S)	P		(A, S)
8		(M, S)	Q	X	(A, S)
9		(A, St)	R		(A, St)
10		(M, S)	S		(A, S)
11	X	(M, S)	-		
12		(M - NA, NS)	T		(A - NA, NS)
13		(M, S)	U	X	(A, S)
14		(M, S)	V		(A, S)
15	X	(M, S)	W		(A, S)
16		(M, St)	X		(A, St)
17	X	(M, V)	-		

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	X	(O, U)

Institutional Veterinarian:

3		(M, V)

Correlates to Version **v6.5** 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

1. The committee reviewed the June 2021 inspection summary.

2. The committee was updated on a lab's use of an instant pot for tool sterilization. The committee informed the lab that it may continue to use an Instant Pot with the biological indicators for the next six months and to provide updates regarding sterilization cycles/results from the Instant Pot. Use of the Instant Pot is not considered a long-term, permanent solution.

3. The committee reviewed a self report in which blood was found in cages after genotyping, in addition to neonates weaned at times that were not approved in their protocols. The lab proposed other genotyping techniques that were not outlined in the protocols. The committee informed the lab that they must submit an amendment to carry out alternative genotyping methods. The committee also requested further details about training and oversight for genotyping and weaning procedures.

4. The committee reviewed a self report in which multiple animals were found dead in their cages with no previous clinical signs. The lab confirmed they will communicate with veterinarians in a more timely matter in instances where unexpected illness or death is observed in animals. The committee considers the matter closed.

5. The committee reviewed a self report in which animals were housed in the lab. The lab confirmed they will no longer keep animals in the lab for over 24 hours. The committee considers the matter closed.

6. The committee discussed an adverse event in which use of an 18-gauge needle to gavage caused death in a subset of animals. The lab switched to a 22-gauge needle and had a veterinarian observe the procedure to ensure animal welfare. The committee considers the matter closed.

7. The committee discussed an adverse event in which the incorrect dose of a paralytic lead to euthanasia of an animal on study. IACUC leadership and RAR veterinarians are meeting to further discuss this incident, historical and recent lab events, and to consider possible next steps for this lab.

8. The committee reviewed a self report in which a room in the vivarium was missed during RAR daily health checks. No animal welfare issues were noted. Animal care supervisors will have a second supervisor review all posted room schedules to ensure no room is missed. The committee considers the matter closed.

9. The committee discussed an adverse event where an animal was found alive after assumed euthanasia. The animal was humanely euthanized upon discovery. The personnel responsible for the incident could not be identified. Animal care supervisors confirmed they will retrain staff in the building on appropriate euthanasia techniques and verification of death. The committee is waiting for further details from other labs that were potentially involved.

10. The committee was updated on a fire that occurred in a building where animals are used. No animals were impacted due to the fire.

1. **IACUC-NEW (# Protocols: 2)**

    1. **Protocol Title:** 2107-39237A A Preclinical Evaluation of an Expandable Pulmonary Valve in a Growing Sheep Model
    Species &Pain Class: (A,B) Sheep (Biomedical)
    Question the Research Addresses: PI requests 10 class A and 40 class B sheep for a study to evaluate chronic device expansion to accommodate somatic growth of the native pulmonary valve annulus in a growing ovine model.

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

    - Is the IMHA SOP current number listed - 1605B378012 Does the SOP cover the care and

management of the ewes nursing lambs and the nursing lambs (if they are going to be potentially housed at [redacted])?

- You've justified the number of ewes (10) indicating twin lambs maybe obtained for the various studies. You may need more ewes if you are planning on using 30-40 lambs for your group studies.

- Please indicate the disposition of the ewes and extra lambs not used in this section-marketing, sales, return to farmer (donation?), etc. You mentioned in the species section about returning to the farmer or marketing but it should be indicated here as well.

- Please check the yes box for the food chain approval (#5) since in another section it was indicated the potential for animals for animals to enter the food chain.

Committee Decision: Stipulations must be met
For: 11 Against: 0 Abstain: 0
Member 1 out

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2. **Protocol Title:** 2106-39208A Transposon Mutagenesis in Vivo (A)
Species &Pain Class: (A,C) Mice
Question the Research Addresses: PI requests 2140 class A and 13897 class C mice for a study asking what gene mutation combinations can cause cancer and what drug or drug combinations can inhibit cancer growth.

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

- 1) In the hydrodynamic injection, why is the eye lubrication being given after the procedure? It should be given as the first thing after induction of the sedation/anesthesia, especially if they are also being placed in a tail vein restraint device. Please update to make sure it is given before the procedure is performed. 2) Do the animals ever reach full anesthesia under this anesthetic regimen? If so, does a restraint device remain necessary to give the injection? It would allow for better animal observation for anesthetic depth and record keeping.

- The attachment for this procedure is quite thorough however, there are some of the Specific Aims (SA) that don't lay out volumes. It would be good to summarize the volumes for all of these SAs in the actual procedure and state that these will be used throughout the protocol so it makes it easier for both staff and reviewers to know what to give each animal. For example: All IP injections: 10 ml/kg; All IV injections 5 ml/kg

- Is there any reason that the analgesia is given post procedure rather than right before? To prevent wind-up pain, it is recommended that the animal receive analgesia before the start of the noxious stimuli. In this case, since it is carprofen during preparation would be a good time to provide the dose.

- There are much less invasive methods to collect blood in rodents, such as facial vein or saphenous veins. Please describe why retro-orbital bleeding is necessary in this project. Additionally, the procedure description (SA9) in the experimental design doesn't include blood draws, thus could this procedure be removed? There is already another blood collection procedure that does not use this more invasive method.

- Please update this section to more clearly write the dose for mice receiving the chow. In the current iteration, there is a mix of both fluid and diet doses making interpretation difficult, especially since this is a diet only procedure.

- Please update the monitoring parameters for neonatal mice to add a parameter to assess depth such as

a lack of movement and response to a gentle paw pinch.

- In all surgical procedures, it is noted that isoflurane is listed at only one percentage (3% in O2), however, this may be too high of a percentage to keep animals under during all procedures. To prevent overdosing, it would be better to list a range of isoflurane percentages to allow for more control over anesthesia. Recommend replacement for all procedures with 1-3% or even higher for induction.

- For redosing animals under ketamine/xylazine anesthesia, only use ketamine at approximately 1/3 the original dose. Dosing with xylazine a second time can significantly increase anesthesia time and lead to anesthetic complications. Please change the redosing accordingly.

- Please change the eye lubrication application to immediately prior to procedure. As stated it will occur after the procedure which is not appropriate to keep the eyes lubricated during the entire anesthetic event.

- The total dose for both lidocaine and bupivicaine are much higher than recommended as a local anesthetic (4 mg/kg max total for lidocaine and 2 mg/kg max total for bupivicaine). Please update these doses to prevent an overdose of these agents. Please verify these agents will be given at the site of surgery as they are a local anesthetic. It would be best to give the injection to the surgical site prior to incision rather than at the end to get the most benefit. It is noted that the analgesic regimen for this procedure has continued injections with both lidocaine and bupivicaine daily after the procedure. These drugs are fairly short acting and are appropriate to give as multi-modal analgesia at the time of surgery, however, once daily injections to the area will cause more distress and possible trauma to the healing area. Please remove the daily injections after the initial doses. If multi-modal analgesia is desired, adding a NSAID such as carprofen (5 mg/kg, SC, once daily) or meloxicam (2 mg/kg, SC, once daily) as a daily analgesic is recommended.

- Please update Section 3 of the health and monitoring to make sure listed treatments match what is listed in the experimental design/procedures. For example it states that buprenorphine will be given after SA2, however, this is not listed elsewhere and the surgical procedures now have sustained release buprenorphine as the main analgesic.

- Due to the significant surgical procedure, it is recommended that carprofen (5 mg/kg, SC, once daily) or meloxicam (2 mg/kg, SC, once daily) be added as an adjunct analgesic. Initially it could be given at the end of the procedure as a one time dose to help immediate post-op pain in combination with the buprenorphine and then on an as needed basis for the following 3 days for break through pain noted.

- Overall, your SOPs look good, but many of the links in them are broken. See below for some updated links to replace. Also, please make sure the chemical name is correct throughout each document, and ensure that each statement still applies. Toxic Hazard Class SOP template: https://dehs.umn.edu/node/129581/attachment Chemotherapy Fact Sheet: https://dehs.umn.edu/node/129261/attachment Chemical Waste Guidelines (formerly the Chemical Waste Guidebook): https://dehs.umn.edu/8-chemical-waste-guidelines Clinical Services: https://bohd.umn.edu/clinical-services Respiratory Protection Program: https://dehs.umn.edu/respiratory-protection

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

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2. IACUC-AMENDMENT (# Protocols: 1)

1. **Protocol Title:** 2012-38674A "Investigating the neural mechanisms underlying motivation and emotional processing using mouse models" "Determining the unique and dynamic neural constellation belonging to acute and chronic stress states" "Stress-induced modulation of striosome circuit in decision making"
Species &Pain Class: (A,B) Mice
Question the Research Addresses: PI requests the following changes to the protocol: 1. Addition of a new early life stress model called the "Limited bedding and nesting" or LBN model. Edits have been made to the Procedures, Experimental Design and IACUC table sections. We are requesting a small increase in mice - enough to run a pilot study. Should the pilot study work, we will request a larger cohort of mice. 2. Use of the inhaled anesthetic, isoflurane for non-survival transcardial perfusions in a subset of animals being used for cfos immunohistochemistry. Edits have been made Procedures/Other/Transcardial perfusion tab and IACUC table attachment. 3. Edit the dimensions and timing of the light/dark box to represent the recently acquired Stoelting apparatus.

Committee Decision: Approved as submitted
For: 12 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee
Minutes
VCRC - 76D

Meeting Convened: 12:00PM	Quorum Requirement: 9
Meeting Adjourned:	Members Present to Vote: 11

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v6.5** 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:

1. The committee was informed of the upcoming Semi-Annual Program review, scheduled for 10/19/21, and encouraged to attend and participate.
2. The committee discussed a preliminary reinstatement plan submitted by an investigator whose animal use privileges are currently suspended. The committee was satisfied with the responses and the lab's history specifically related to their use of rodents, and voted unanimously to reinstate the investigator's rodent protocol. The committee felt that the responses related to the use of cats were not yet sufficient. A meeting will be scheduled with the investigator to discuss the lab's history, the model, and the corrective action plans; all committee members are invited to attend.
3. The committee discussed a proposal to allow Veterinary Medical Center anesthesiology residents and faculty to participate in anesthesia of research animals. VMC staff would be added to the RAR Roster protocol to track occupational health and training requirements and sign a confidentiality agreement, and investigator permission would be obtained in advance. The committee voted to accept this proposal.
4. The committee discussed the IACUC office's request for permission to take advantage of OLAW guidance providing the flexibility to conduct inspections of non-USDA areas with only one member. The standard would remain to use two members when possible. The committee voted to approve this proposal.
5. The committee discussed whether IACUC approval is needed for a project that does not involve university-owned animals, university personnel, or university facilities. After consultation with the Office of General Counsel and verification that the grant does not require an IACUC protocol, the committee voted not to require a protocol for this project. The submitted protocol will be withdrawn.
6. The committee discussed classification and reporting of wild animals as USDA-covered species. Currently wildlife undergoing invasive procedures are being included in our USDA report, but there is a lack of clarity on which procedures should be considered invasive. A subcommittee will be formed to develop clear definitions and policy around which procedures would be considered invasive and therefore non-exempt from USDA categorization.
7. The committee was updated on the availability of pentobarbital-containing euthanasia solutions. The previous shortage appears to have resolved, therefore the exemption to use pentobarbital-containing euthanasia solutions for up to 3 months past the manufacturer's expiration date will be allowed to expire on 9/15/21. In date solutions must be used after that time.
8. The committee discussed a self-report in which toe clipping of neonatal mice whose toes were still webbed resulted in the removal of more than the allowed single digit per foot. The lab was reminded of the IACUC's policy on toe clipping, and going forward, will not attempt to clip toes if they are still webbed. An amendment will be submitted if the lab decides on an alternative method. The committee endorsed the corrective action plan and considers the matter closed.
9. During review of a protocol, it was decided that a subcommittee will be formed to allow for further discussion of and development of updated policies and guidelines related to the use of SR-buprenorphine institution-wide.

IACUC-R1S1(# Protocols: 14)

IACUC-R1S1 - NEW(# Protocols: 10)

1. **Protocol Title:** 2108-39311A Long Term Evaluation of a Bioabsorbable Conduit in the Sheep Model.
   Species &Pain Class:(A,B) Sheep (Biomedical)
   Question the Research Addresses: The purpose of this study is to evaluate the developmental conduit material in a long term animal model. This test article will be implanted and evaluated in a chronic sheep mode to determine the biocompatibility of the material as it is absorbed for up to 3 years.

   The committee concurs that this protocol can be approved via designated member review once the following

stipulations are addressed by the PI:

Comment: Please consider adding standard buprenorphine (including dose and route) to the analgesic agents table as you are planning to use it in case of breakthrough pain.

Comment: In the experimental endpoints section you state that the animals may be maintained on this protocol for 140 +/-10 days; however, in the experimental design section it is written that one of the groups (n=4) is survived up to 3 years after surgery; please reconcile.

Comment: Both the RVOT reconstruction and the Interpositional Pulmonary Conduit Surgery procedures mention the IV use of ceftiofur (I think this is the preferred route of administration) but it is only listed as SQ/IM in the surgical procedure description in the procedures section. Please update.

Comment: Admittedly I am not a cardiothoracic surgeon but I am unsure why there are two separate procedures (RVOT reconstruction and the Interpositional Pulmonary Conduit Surgery) listed in the attachments section. These two documents seem redundant. I thought the RVOT procedure is what best describes what you intend to do.

Comment: Termination procedures document lists "intra cardiac echo" but in the "procedures" section it is mentioned that this procedure may be performed on animals that will be recovered subsequently. Attachment or documentation describing this procedure in animals to be recovered after the procedure is missing; please add.

Comment: Please indicate an acceptable range for body temperature, and what will be done if temperature is outside of that range.

Comment: The procedures refer to decrease anesthesic agent and increasing IV fluid administration. Please indicate how blood pressure indications will guide fluid administration, and the range of acceptable IV fluid administration (the protocol currently refers to a fixed 10 ml/kg/hr).

Committee Decision: Stipulations must be met
For: 9 Against: 0 Abstain: 0
Member 1 out

2. **Protocol Title:** 2108-39345A Evaluation of a novel arterial cannula to be used for extracorporeal circulation
   Species &Pain Class:(B) Sheep (Biomedical)
   Question the Research Addresses: The purpose of this study is to assess the deliverability and use of the TFA device in a sheep model.

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

   Comment: In the anesthetic agents list in the "Sheep Acute Testing" procedure portion of the protocol, propofol is listed at a dose of 1-2mg/kg; In the attachment describing the procedure, propofol is listed in table 3, "Induction Medications" to be used at a dose of 2-6 mg/kg. Please adjust for consistency between the sections.

   Committee Decision: Stipulations must be met
   For: 9 Against: 0 Abstain: 0
   Member 1 out

3. **Protocol Title:** 2105-39125A [redacted] Animal Tech Training
   Species &Pain Class:(B) Mice; (B) Rat
   Question the Research Addresses: Not applicable
   Committee Decision: Approved

For: 10 Against: 0 Abstain: 0

4. **Protocol Title:** 2107-39251A Deep Brain Stimulation with Electric Rotating Fields
Species &Pain Class:(B) Rat
Question the Research Addresses: We will validate and optimize our novel amplitude modulated pulse paradigms which generate alternating electrical fields to modulate the activity of specific neuronal populations, and we will compare their efficiency, flexibility and selectivity with conventional DBS strategies which utilize square pulses in the 10-300 Hz frequency range.

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

Comment: Including the expected drop out rate of 20% of animals in the study, the table in the experimental design section of the protocol describes the need for up to 395 rats. Please adjust the total number in this table to 395, and the number of requested animals in the "species" section of the protocol to 395.

Comment: Please include a procedure for the "spared nerve injury" described in the experimental design, or remove from the experimental design if it will not be done.

Comment: The expertise of Dr. Fairbanks is referred to - what is the role of that team in your project. Dr. Fairbanks does not appear to be on the study team, nor are any of her staff. This then begs the question as to who will be performing the SNI surgeries and the von Frey testing. If these will no longer be done, please remove the references.

Comment: Please complete the surgery section for the Spared Nerve Injury, or remove the references to this if it will no longer be done.

Comment: Part 1 - Experiment 1 reads: "Implantation of high density 256 channel leads to any area of the brain, e.g. the infralimbic cortex (IL area) STN- subthamamic nucleus/area, prelimbic cortex, entorhinal cortex, medial septal nucleus - passive system, i.e., connected with flexible cables to the board". Please update the protocol to explain the purpose of implanting channel leads 'into any area of the brain'. What is the purpose of this experiment?

Comment: Part 1 - Please update the protocol to indicate how many animals will receive neuronal tracer injections.

Comment: Part 4 - This section includes both survival and non-survival. Will the survival animals have any implants or other interventions or will they just undergo fMRI similar to the survival animals in Part 3? Please update the protocol to clarify.

Comment: The SNI model is very stable after the first few days. The PI should consider reducing the number of von Frey tests over the 2 week period - daily is not recommended as it will cause unnecessary stress to the animals. Something like days 3, 7, 10 and 14 are suggested. If this will no longer be done, please remove references.

Comment: Section 5 includes ".....and we will stimulate spinal cord during different stimulation strategies for comparison on the bench and during simultaneous MRI...". Please clarify what you mean by 'on the bench'. In that experiment please indicate the timing of the morphine injection.

Comment: Section 6 requires additional information. In addition to noting 'animals may have DBS, SCS or both....and allowed to recover up to three months' indicate how many you expect, what implants they will have and why you are doing this extended recovery time. Section 6 also notes that some DBS or SCS stimulation will be delivered via these survival implants in awake animals. How many animals will this be performed in? What will be the experimental and clinical endpoints? How will you ensure, for example, that the stimulation parameters are not pro-nociceptive?

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0

5. **Protocol Title:** 2107-39262A Phenotyping Study Protocol
Species &Pain Class:(B) Mice
Question the Research Addresses: What are the genes that influence mammalian lifespan, cancer risk and the age at onset of degenerative diseases.

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

Comment: Please add a Tumor Induction procedure to capture IACUC specific questions related to tumor burden monitoring. Within this procedure please clarify the maximum tumor size, which is mentioned as 4.2 cm3. IACUC guidelines call for a 2 cm3 limit unless an exception is requested.

Comment: Based on language in your Experimental Design attachment ("Under this experimental procedure we will evaluate “fomite transfer” as to their suitability to achieve the above objective. The motivation is to reduce the variability associated with the immune maturation in “cohousing with [redacted]” procedure.") it sounds as though SPF mice will only be exposed to fomite bedding. Will they also be co-housed with [redacted] mice?

Comment: There is a weight loss cutoff of 25% in endpoints for project 1, but a 20% cutoff everywhere else. Please update the protocol to explain or reconcile this difference.

Comment: Please update the protocol to define SPC-Cre mice used for project 3.

Comment: Please update the protocol to define the need for the CD45.1 mouse line for project 4.

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0

6. **Protocol Title:** 2107-39297A True metabolizable energy content of feed ingredients for poultry
Species &Pain Class:(B,C) Turkey; (B,C) Chicken
Question the Research Addresses: The data collected helps to confirm or provide information on differences for metabolizable energy within ingredients and among different ingredients.

Committee Decision: Approved
For: 10 Against: 0 Abstain: 0

7. **Protocol Title:** 2106-39189A Acute renal nerve activity and modulations in hypertensive sheep
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This research works to address the mechanism and importance of the neural-cardiovascular-renal interaction in the development and maintenance of hypertension.

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

Comment: Description of the open and closed loop e-block is missing under the subheading "procedures". It describes 1: "DOCA, Transmitter implant, and Modifications to diet and drinking water:" and 2: Acute procedures (including RDN and Sham procedures). Please add this to the protocol. .

Comment: Under the justification for Animal Numbers heading the protocol describes "group sizes of n=36." I am not sure if this is typo, but previously the protocol stated that the number of animals in the RDN and sham

groups will be 5 and in the two e-block groups n=10. Please update the protocol to clarify.

Comment: The protocol states: "Please see attachment entitled "Acute/terminal procedures" for procedural description." There is no attachment that matches the above title. I think you might be referring to the attachment entitled "term procedure FINAL"--please clarify.

Comment: I think the surgeries "Terminal procedures" and "Unilateral and bilateral Kidney Denervation; Sham procedure" refer to the same interventions thus one of them are redundant. Please clarify.

Comment: As per previous reviewer, the Health and Monitoring section needs to be updated. Remember, responses to question 1 should highlight potential health concerns for al procedures on the protocol. Please incorporate your justification for single housing sheep on this protocol in response to question 5.

Comment: As other reviewers have stated, please update the text under justification for number of animals. Right now it reads that n = 36 for a pilot study, but really your group sizes are n's of 5 and 10. While it is common to ask for an additional ~10% number animals in case of unexpected adverse outcomes, you're asking for 6 (~16%) additional sheep. If you're expecting a higher mortality rate, please elaborate.

Comment: I'm not sure I understand how housing sheep individually will allow them to become hypertensive. Is the concern that they aren't eating enough when group housed? Could they be fed separately but still housed together overnight? Or multiple salt licks added to the pen? Perhaps the sentence should be updated to say "sheep could have their intake monitored if the expected rise in blood pressure is not observed and this might result in the need to be temporarily housed alone."? You say that sheep will be a fed a high salt diet and given high salt water for up to 1 yr, but this study is only 40 days. While weight is a good indicator of dehydration, you should also check moistness of the mucus membranes and whether or not their eyes are sunken.

Comment: In response to "How long will animals be maintained after surgery?" you state "Animals will be maintained for maximally for up to 1 year on this protocol....Animals may undergo US examination approximately every month or if there is a clinical need." but based on the Experimental Design it sounds as though though sheep are maintained 30 days post transmitter implant and you do not have ultrasound examination in the Experimental Design section or anywhere else on the protocol.

Comment: Again you state that animals will be maintained up to 1 year on this protocol, which doesn't answer the question on how long animals will be maintained following surgery.

Comment: Why does your literature search only go until April 2020? Don't you want to know if there are more recent articles available to hep refine your procedure and potentially improve the quality of life for these animals? Please update you search.

Comment: Since ultrasound is not a procedure listed on the protocol, I'm not sure why you have done an alternative search for this. The same is true for capsaicin -- is this being administered on this protocol? Both of these documents should be removed. Your other literature search documents have the wrong protocol and appear to have search terms for chronic surgeries and thoracic surgical approaches, neither of which are described on this protocol. Please perform an appropriate literature search and update the protocol.

Committee Decision: Stipulations must be met
For: 9 Against: 0 Abstain: 0
Member 1 out

8. **Protocol Title:** 2107-39273A Cancer Immunotherapy using Antisense microRNAs Molecular mechanisms that orchestrate colon cancer progression MicroRNA mediated intercellular communication in the activation of T cells Mechanisms of colon cancer progression and novel therapies
Species &Pain Class:(A,B) Mice; (A) Mice
Question the Research Addresses: Extracellular vesicle secreted from colon cancer cells transfer into T cells,

resulting in deficient T cell activation and impaired anti-cancer activity.

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

Comment: Given the potential for the following: "Tumor growing might cause pain/distress resulting from bloody stools or rectal prolapse" is proposed monitoring plan sufficient? Also how are the outcomes of bloody stools or rectal prolapse addressed if those arise?

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0

9. **Protocol Title:** 2107-39254A ECMO Training for Physicians and Emergency Personnel
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: This is a training course for the purpose of training physicians and emergency personnel on how to use ECMO for resuscitation using an animal model of cardiac arrest.

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

   Comment: In the experimental design section of the experiment, it is described that furosemide (2-6 mg/kg, IV) may be administered during the ECMO procedure if pulmonary edema occurs. Please add furosemide to the list of "other support agents used during procedure" in the ECMO procedure section of the protocol. Please also add pulmonary edema to list of anticipated specific study-related adverse health conditions in the "health and monitoring" portion of the protocol.

   Committee Decision: Stipulations must be met
   For: 10 Against: 0 Abstain: 0

10. **Protocol Title:** 2107-39284A Use of Inhaled Argon During Hemorrhagic Shock
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: PI requests 24 class B pigs for a study to examine whether use of inhaled argon will offer organ protection in a porcine model of hemorrhagic shock.

    The review of this protocol was Moved to another meeting due to reviewer absence.

IACUC-R1S1 - AMENDMENT(# Protocols: 4)

1. **Protocol Title:** 1908-37333A Laboratory Teaching in PHSL 3051: (Human Physiology), (INMD 6814: Human Physiology or PHSL 5101: Human Physiology), and PHSL 6051: Systems Physiology
Species &Pain Class:(A,B) Rabbit; (A) Rat; (A) Frog (Other)
Question the Research Addresses: Some specific physiological concepts are best illustrated through the use of animal tissue.

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

   Comment: This request is for video to be saved on a phone in case labs can't be held in person in the future. It seems likely that there's plenty of educational video material available showing basic principles of physiology. Please update the protocol to provide additional justification for using this video versus existing educational videos.

   Comment: There may be important reasons why the video of the procedure as it is performed in class may be necessary to the educational goals of that class. That said, the PI needs to be aware (if the PI is not already aware)

that the recorded video of the procedure will be subject to Freedom of Information Act requests. Therefore, the team member (Bill Klein) will need to be aware that the video residing on his personal cell phone may be requested and will need to be provided if so requested. Both the PI and the team member should acknowledge that they understand the potential that they will need to provide the video to the public if a member of the public so requests.

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0

2. **Protocol Title:** 2106-39205A Cerebral circulation mapping in the sheep model
Species &Pain Class:(B) Sheep (Biomedical)
Question the Research Addresses: This study aims to map the cerebral vascular anatomy of the sheep brain using the latest in clinical imaging, which may include computed tomography (CT), magnetic resonance imaging (MRI), transcranial Doppler ultrasound, and fluoroscopy.

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

   Comment: Please describe the distances and the procedure for transporting across the different procedural sites.

   Comment: Please include the purpose and a description of the microspheres in the Rationale and/or Experimental Design.

   Committee Decision: Stipulations must be met
   For: 9 Against: 0 Abstain: 0
   Member 1 out

3. **Protocol Title:** 2001-37750A Preclinical Evaluation of the Tolergenic Efficacy and Safety of Apoptotic Donor Leukocytes and Induction Immunosuppression with DFI105, Rapamycin, Etanercept, and Tocilizumab for Islet and Kidney Allotransplant in Nonhuman Primates
Species &Pain Class: (B) Nonhuman Primate (Macaques)
Question the Research Addresses: The study has not yet initiated and the study design is altered based on trial results from completed mechanistic trial 2008-38343A “MAMISOT: Mechanistic evaluation of expanded apoptotic donor B cells in solid organ versus cellular transplantation” and pre-IND planning with FDA. PI requests the following changes: ASKP1240 (xCD40mAb) is being replaced with DFI105 (xCD40mAb). Group B (previously islet cell transplant without xCD40mAb) is being replaced with solid organ kidney transplant recipients receiving xCD40mAb. Additional surgical personnel have been added to support kidney transplants. Blood collection procedure simplified to total volume collected (details of what is collected in appendix versus creating individual procedures). Animal numbers have been reduced, as backup donors at a 1:1 ration are not needed for solid organ (kidney) transplant recipients.

   The review of this protocol was Moved to another meeting due to reviewer absence.

4. **Protocol Title:** 1911-37613A Reprogramming astrocytes into neurons in canine stroke model
Species &Pain Class:(B) Dog
Question the Research Addresses: Can astrocytes reactive after stroke in canine be reprogrammed into neurons?

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

   Comment: At the end of the 4th paragraph it states that if the catheter is removed, it will be administered via IP stick, is that a typo and supposed to say "IV" stick? If so please correct.

   Comment: Please incorporate your responses related to BrdU administration into the Experimental Design section. Explain the decision process for when dogs may/may not receive the injection. Ultimately it should be

clear to reviewers what happens to dogs once they are enrolled on this protocol and that treatment groups are randomized.

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0

Institutional Animal Care and Use
Committee Minutes 9/21/21
VCRC - 76D

Meeting Convened: 12:00 PM	Quorum Requirement: 9
Meeting Adjourned: 1:51 PM	Members Present to Vote: 12

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v7.0** 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:

1. The committee continued an ongoing discussion regarding a PI whose use of cats has been suspended, including the most recent corrective action plan submitted by the PI. The committee understands the PI's rationale for the use of the species but has continued concerns about the age of the animals used and the role this may play in complications that have occurred. Additional information will be requested from the PI regarding consultations that the lab has had or plans to have with experts in the field, the proposed age and size of animals to be used, and protocol updates that will be needed. The committee will also request consultation from experts in veterinary anesthesiology. The suspension of the PI's use of cats remains in place until further notice.
2. The committee was updated on the August inspection summary.
3. The committee was updated on the rescheduling of the fall Semi-Annual Program Review; the new date is 11/2/21.
4. The committee reviewed additional responses submitted in response to a self-report involving improper tail snipping of mice. The PI submitted an updated SOP for genotyping and a plan for ensuring lab staff are trained. The committee has no further concerns and considers the matter closed.
5. The committee was notified of a continuing education opportunity, the Animal Research Oversight Course through PRIM&R. There was interest in the course and the IACUC office will arrange an institutional subscription.
6. The committee was updated on the veterinary pre-review process.

Panel: FCR Panel
September 21, 2021

1. **IACUC-R1S1(# Protocols: 11)**

    1. **IACUC-R1S1 - NEW(# Protocols: 10)**

        1. **Protocol Title:** 2108-39363A Omental Bioreactor for Esophageal Tissue
        Species &Pain Class:(B) Rabbit
        Question the Research Addresses: PI requests 12 class B rabbits for a study to examine whether the omentum promotes growth and vascularization of a tissue engineered esophagus.

            Committee Decision: Approved
            For: 10 Against: 0 Abstain: 0
            Members 1, 10 out

        2. **Protocol Title:** 2106-39206A Evaluation of a Novel Heart Valve in the Tricuspid Position in the Sheep Model
        Species &Pain Class:(A,B) Sheep (Biomedical)
        Question the Research Addresses: PI requests 30 class B sheep for a protocol that will be used to evaluate developing a transcatheter tricuspid valve system.

            Committee Decision: Approved
            For: 10 Against: 0 Abstain: 0
            Members 1, 10 out

        3. **Protocol Title:** 2108-39343A Preclinical Evaluation of a Novel Mechanical Heart Valve in the Sheep Model
        Species &Pain Class:(B) Sheep (Biomedical)
        Question the Research Addresses: PI requests 24 class B sheep, which will be used to evaluate the biocompatibility, functionality, durability, and safety of a developmental heart valve.

            Committee Decision: Approved
            For: 10 Against: 0 Abstain: 0
            Members 1, 10 out

        4. **Protocol Title:** 2105-39116A Endovascular Embolic Training Model
        Species &Pain Class:(B) Pig (Biomedical)
        Question the Research Addresses: : PI requests 24 class B pigs to be used for a training course for the instruction of new endovascular surgical neuroradioloists in abnormal vascular malformations (AVM) and aneurysm embolization.

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

            Comment: Please include a more detailed description (new Procedure Tab) of the embolization procedures that trainees will be performing.

            Comment: Since this is a training protocol, please check the box for Teaching on the Rationale page, and provide either a course number or other information related to the training.

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

        5. **Protocol Title:** 2108-39378A APOBEC Proteins in Chemically-induced Cancers

Species &Pain Class:(A,C) Mice
Question the Research Addresses: PI requests 5787 class A and 400 class C mice for a study to examine whether APOBEC deaminase activity contributes to the progression of chemically-induced tumors in vivo.

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

Comment: The animal number requested in Species section does not match the animal number requested in the Experimental Design and Procedures sections. In the Species section, the protocol requests 5787 animals in Pain class A and 400 animals in Pain class C. However, in the Experimental Design and Procedures sections, the protocol only requests 80 animals for experiments (Pain class C) and 220 animals for breeding (Pain class A). Please update the appropriate sections to reconcile the numbers.

Comment: The Experimental Design section states that genotypes will be determined via tail snips from pups "approximately" 21 days of age, but the protocol does not include a procedure for this process. Please add a separate procedure for tail snips and review the IACUC guideline on rodent tail biopsy procedures. Note that the procedure is recommended for mice 10-21 days of age and that disinfection of the tail with alcohol prior to the procedure is required. Local anesthetics are encouraged for the procedure in mice aged 10-21 days, and either local or general anesthesia is required for this procedure with mice over 21 days of age.

Comment: Please add to the protocol a copy or description of your body score condition guide, either in your tumor induction procedures or as an attachment to the protocol.

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

6. **Protocol Title:** 2108-39342A Algorithms for programming deep brain stimulation systems for essential tremor
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: PI requests 9 class B NHPs for a study to investigate the current steering abilities of a directional deep brain stimulation (DBS) arrays implanted in the thalamus of non-human primates. This study will examine how targeting specific brain pathways affects thalamic, cerebellar, and motor and sensory cortex activity, and how one can use computational models and optimization / machine learning algorithms to predict the spatiotemporal network dynamics resulting from spatially targeted DBS for treating Essential Tremor.

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

Comment: For the physical restraint procedure, you only describe using a boxchair despite having pole/collaring elsewhere in the protocol. I am confused by the current statement " The box chair does not require a collar on the animal and the transport process involves using a jump box directly into the box chair, which is a refinement from previous pole and collar methods of non-human primate restraint. We have transitioned all our animals to the box chair method." Please justify the use of pole/collars on this protocol. If they are used, you should update the Physical Restraint procedure to include pole/collar chair language.

Comment: Please update your response to "Indicate the duration of restraint" to include the maximum amount of time an animal would be chaired AND the maximum amount of time an animal would be posted. Please note that the USDA Animal Welfare Act states: "In instances where long term (more than 12 hours) restraint is required, the nonhuman primate must be provided the opportunity daily for unrestrained activity for at least one continuous hour during the period of restraint".

Comment: Your response to "If the animals do not acclimate or if they show forms of distress, what course of action will be taken?" should include a plan to retrain the NHP to chair restraint. The veterinarian should be notified in instances where chamber maintenance is required in NHPs refusing to cooperatively enter the chair so that they can help determine a safe sedation/cleaning schedule.

Comment: Please add that a veterinarian will be contacted if skin abrasions related to collar placement are seen and that you will work with them to determine a topical treatment plan and if/when to remove the collar to allow for healing.

Comment: I do not think there is sufficient justification for food restriction in NHPs, given that you have an extensive cooperative training program and are requesting fluid restriction on your protocol. I do think the idea of altering when they are fed could be appropriate, and request the following changes to the protocol. 1. Please select "modified" instead of "Restriction" 2. Remove all language about feeding <100% of daily biscuit ration. Animals should be fed their full biscuit and produce ration every day. 3. Better describe how scheduling would work. RAR typically feeds NHPs twice daily, but with this setup it may be beneficial to feed animals once at the end of their training period. The risk of bloat/overeating is lowed since monkey will be fed food rewards throughout the day. 4. NHPs should still have a baseline weight and continue with weekly weighing while on food scheduling. 5. In response to impacts that this manipulation may have on the animal, hunger and bloat are the most likely. Additionally there could be distress related to an altered feeding/husbandry routine. Animals are still fed throughout training, which should decrease hunger and bloat risk. Potential distress associated with not being fed along with other NHPs in the room will be reported to vet staff. 6. Include that lab and RAR will both provide food and water. I'm not sure if it let's you select both, but you can describe it above if needed. This is important given that RAR staff [redacted] and the animal may come back afterwards -- at that time it is the lab's responsibility to ensure NHPs have been fed their daily ration.

Comment: In the description of dietary manipulations, it is described that if the animal loses >10% weight over a two week period, it will be evaluated and food restriction will be stopped; in the expected impact section, it is described that if the animal weight falls below 5% of previous weight over a week, food restriction will be stopped. Please clarify for consistency which of these guidelines will be used for determining if food restriction effects need to be evaluated.

Comment: Please update the imaging procedure to state how much time will be allowed between repeat imaging procedures (e.g., in the case of poor image quality during a previous imaging session)

Comment: Right now the protocol reads "Animals that are fluid restricted will be restricted up to 7 days per week" -- what is the maximum number of days, or weeks, they could be restricted for in a row? 2 weeks? 2 years? You state "The animals will be provided ad libitum water two days before survival surgery and for at least 3 days following surgery. " but this should apply to any sedation event. Please edit. In general you should provide more detail on when you decide to fluid restrict an NHP. What steps are taken first? Consider positive reinforcement training with food, using juice/gatorade/koolaid (while on full water), using smoothies/yogurt (while on full water) etc. While there may be situations where fluid restriction is required, the protocol should clearly outline the process. Another good indicator of sub-clinical dehydration is poor appetite. Please add that you will monitor biscuit intake in addition to the other parameters listed while NHPs are fluid restricted. Include that RAR and lab staff may both be responsible for providing water.

Comment: Your behavioral training document needs to describe steps taken if animals are regressing or failing to progress to the next step. Right now it describes using a pole and collar for NHPs that fail to progress with box chair training but you cannot use force with a pole and collar -- the NHPs MUST be cooperatively trained for physical restraint regardless of the method used. Please add a statement on how you address regression or signs of distress during behavioral training. Note, a lot of groups will go back to an earlier stage of training that the NHP is comfortable with and "start over" from there.

Comment: Please remove "reducing daily biscuits". See previous comments on food restriction under Food/Water Scheduling.

Comment: Please confirm that you will comply with IACUC Policy/Guidelines on Photography, Video and Audio Recording of Animals Use in Research and Teaching.

Comment: For the Drug Table attachment - You list MPTP, but I do not think you are administering MPTP on this protocol. - Ketoprofen and Ibuprofen are not recommended as an NSAID. Meloxicam/metacam and carprofen are better options. Recommend removing these from the table. - Note that Metacam is just a brand name for Meloxicam. You can consolidate these lines in the table, if you want, to say "0.1 - 0.1 mg/kg PO/SQ" - Please remove the "cross" symbol from the document and listed alternative routes in the table itself. Currently some of the drugs with the cross cannot be given both IV/IM. - Consider adding a "Frequency" column. For drugs that are dosed per DVM recommendation or as clinical signs develop, you can write "PRN". - The APV drug formulary lists Acepromazine doses at 0.01 - 0.1 mk/kg SQ/IM/IV - The APV drug formulary lists Diazepam at 0.5 - 1.0 mg/kg IV, or 0.5 - 2.0 mg/kg per rectum - The APV drug formulary lists Ondansetron at 0.1 - 0.3 mg/kg IM/IV - The APV drug formulary lists Ceftiofur (powder) at 2.2 mg/kg IM - The APV drug formulary lists Cephalexin at 20-30 mg/kg PO (not IM!) - The APV drug formulary lists Doxycycline at 2.5 - 5.0 mg/kg PO (not IM!) - The APV drug formulary lists Roecephin (Ceftriaxone) at 25-50 mg/kg IM/SQ/IV - The APV drug formulary lists Mannitol at 0.5 - 1.0 grams/kg IV (you currently have mg) - The APV drug formulary lists Dopram at 1.0 - 2.0 mg/kg IV

Comment: The RAR vet staff recently consulted with veterinary anesthesiologists and they do not recommend sedating with atropine. While atropine can minimize secretions, it only stops production of aqueous secretions and still allows for thick, mucous sections to build up. This can actually clog the tubes and do more harm than good.

Atropine should only be used as an emergency drug in NHPs with low heart rates. They also recommended against Dexmedetomidine for sedation with prolonged procedures (surgery, MRIs) given the profound negative effects it can have on blood pressure. The benefit of Dexmed is that it can be reversed, which makes sense when you are sedating for a short procedure where you want to hasten recovery. However, since surgeries and MRIs take several hours, it is better to sedate with Ketamine alone. Note: These recommendations apply to all prolonged anesthetic events and will require edits in a few sections of the protocol. Please edit the relevant section. If you'd like to give yourself more flexibility, state that NHPs will be sedation with Ketamine (10mg/kg) or a combination of Ket/Dex.

Comment: Please update your response to "Please describe aseptic technique". - State "We will scrub the area no less than three alternating scrubs with disinfectant (iodine or chlorhexidine scrubs) and 70% alcohol working from the cleanest area to the dirtiest". - Please remove the sentence "Lidocaine may be injected at the incision site." since lidocaine is an alagesic, not an antiseptic. ** This also applies to your Microdrive surgical procedure **

Comment: Please update the first few sentences of the Description section to read.... "The monkey is injected with a dose of Ketamine (10mg/kg) Or Ketamine(3-5 mg/kg) / demedetomidine (0.01-0.02 mg/kg). Once sufficiently dissociated, the monkey is transported to the procedure room and prepped for surgery. This includes clipping the surgical site and placing an IV catheter (saphenous or cephalic). Lidocaine is then sprayed into the larynx and the monkey is intubated and may be placed on a ventilator. Isoflurane anesthesia is administered through the intubation tube, and isoflurane anesthesia (1-5%) continues for the remainder of the surgical procedure. Lidocaine/prilocaine (EMLA) cream is applied to the ear canals and ear bars prior to mounting the animal in the stereotaxic frame. Eye lube is placed in both eyes. Lidocaine/Bupivicaine is injected SQ under the intended surgical site. The surgical site is aseptically prepared as described below. To keep the animal hydrated during and after the surgical procedure, the animal is given intravenous saline solution (5-10 ml/kg/hr) (see Anesthetic tab for IV catheterization details). Mannitol (1.5 mL/kg, 20% solution, IV) may be given ~10-15 min before the craniotomy to prevent brain swelling. Body temperature is kept at 37-38 deg C with a recirculating hot water blanket and/or with warm air blanket. Prophylactic antibiotics may be administered before the first incision (see 'anesthetic regimen' tab). " ** You can then remove the first sentence from the next paragraph. ** This also applies to your Microdrive surgical procedure **

Comment: Please provide a maximum number of chambers an NHP could receive. What is the maximum amount of bone/skull that may be removed?

Comment: Based on the text, it sounds like NHPs undergo a chamber implant, then possibly another procedure to do the craniotomy, and then they may undergo an additional two surgeries? Please provide more detail on when additional surgeries may be performed and what these surgeries entail. Is your plan to place more chambers? Would this happen after the original chamber is already open, and subsequently, infected? ** This also applies to your Microdrive surgical procedure **

Comment: Please add an additional procedure for the craniotomy through an existing chamber procedure since the antibiotic and post-op analgesic regimen may vary.

Comment: For the Analgesic Agents table, please adjust the following text: Meloxicam -- switch to read "Loading dose of 0.2mg/kg will be given SQ at the end of the procedure. Following doses at 0.1mg/kg PO or SQ will be given once daily for 3 days, then PRN in consultation with the veterinarian" Buprenorphine -- switch to read "The first dose is given after anesthesia induction but prior to incision. An additional two doses will be given the day of surgery so that all three doses are spaced 4-6hrs apart. The final dose will be in the evening to allow for overnight coverage. The 4th dose will be given in the morning on post-op day 1, ~12 hrs after the previous dose. " Add Carprofen if you intend to use (it is referenced under the Post-Op section below). You should also add it to your drug table if it remains in the protocol. The dose for Carprofen is 4.4 mg/kg PO/SQ once daily. ** This also applies to your Microdrive surgical procedure **

Comment: Please update your Anesthesia monitoring section to reflect current practices. - Remove language regarding toe pinch and corneal reflex. - Add blood pressure as a parameters (MAP >60) - Change SPO2 to be >95% - Change ETCO2 to be 30-50 ** This also applies to your Microdrive surgical procedure **

Comment: Please change your response to Post-Op 2.A.1.a to state that you will confirm animal is able to breathe independently before extubation. Also add that catheters will be removed and hemostasis achieved prior to placement in the home cage. Please edit the text regarding Buprenorphine and Meloxicam dosing to reflect previous recommendations. Your standard antibiotic choice should be 20mg/kg Ceftiofur (Excede) SQ once every 7 days for for 7-14 days. As you can see, the other antibiotics require injection daily, or multiple times a day, which is why Excede is a nice refinement. ** This also applies to your Microdrive surgical procedure **

Comment: Please confirm whether or not the Repair procedure is intended to apply to animals who lose implant integrity secondary to an infection.

Comment: For the Large Cage attachment, please address the following. - Confirm that if paired NHPs fought

while in the large play cage you'd be able to break up the fight. - State that you will follow manufacturer recommendations on contact time for DMQ to ensure appropriate sanitation. - The large cage should be sanitized between monkeys, not just at the end of the day. Apart from the potential effects scent marking could have on their behavior, the cage should be sanitized when different species are using it on the same day or animals from different rooms/building are using it on the same day. Implanted animal should also be in a sanitized pen given their high risk of infection.

Comment: Please add a statement that all NHPs will be screened for microchips prior to undergoing an MRI. Screening includes taking an xray, or doing a full body CT, to confirm that monkey is not chipped. If a microchip is found, vet staff should be contacted to discuss options for removal.

Comment: Please remove the following sentence "Atropine is given to reduce respiratory secretions. Dexamethasone may be used to prevent laryngeal swelling." Atropine should only be used to treat low heart rate and Lidocaine/Cetacaine is sprayed on the larynx prior to intubation, not Dexamethasone. For consistency, change your EtCO2 range to 30-50 and your SPO2 to be >95.

Comment: Are dura scrapings really occurring 5/week? Is 5FU really being applied 5x/week? This seems a bit excessive. APV Guidelines describe 5FU 3x/week. Please confirm that you will ensure the dura is intact prior to using 5FU. Review APV Guidelines on Cranial Implant Care and update the protocol accordingly. This includes a description of how the chamber/parts are handled (aka - via aseptic technique), how often the caps/screws are swapped out and autoclaved, how the implant margin is maintained and kept free of crusts/hair, options for cleaning the chamber itself, etc. Consider adding this as an attachment.

Comment: Because we have seen some significant side effects associated with Harmaline injections, please state that you will start at the low end of the dose range and gradually increase doses until you reach the desired effect. I believe there are also dietary restrictions for animals undergoing harmaline injections (low tyramine diet) so you should address how that is handled. Lastly, please comment on what you do in instances of persistent nausea -- are you monitoring for dehydration? Are you able put a visual barrier on the front of the cage to help dim the light? The side effects/monitoring can be described with the procedure or in the Health and Monitoring section of the protocol.

Comment: Consider using a topical analgesic (e.g. EMLA cream) prior to placing electrodes IM. Please confirm that the chamber are cleaned prior to microelectrode placement below the dura. A clean chamber helps prevent accidentally dragging bacteria beneath the dura and into the brain.

Comment: You have a lot of drugs listed here, but it isn't clear what the "standard" plan is and when one protocol may be chosen over another. Note that cephalexin, naxcel, excede, and rocephin are all the same class of antibiotics -- Excede is the superior choice as it really cuts back on the number of injections an NHP must undergo to dose it appropriately. When would you decide to use Dexamethasone? Is this in consultation with veterinary staff?

Comment: Do you really intend to jacket NHPs? Are you acclimating the NHPs to the jacket? Are you sedating them to put the jacket on? In what circumstances would an NHP be jacketed? What is the maximum amount of time a monkey may wear a jacket/bonnet?

Comment: In addition to what you have written, consider pain/distress associated with collar placement and physical restraint and generalized CNS signs associated with brain swelling, brain abscessation, etc. Update the Health and Monitoring section to reflect appropriate drug regimens and doses.

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

7. **Protocol Title:** 2108-39313A Animal Physiology Laboratories
Species &Pain Class:(B) Bull Frog; (A) Weakly electric fish; (A) Fish (Zebra fish); (A) Bait fish
Question the Research Addresses: PI requests 180 class B bull frogs, 30 class A weakly electric fish, 60 class A zebra fish, and 60 class A bait fish for comparative animal physiology course Biology 3760.

   Committee Decision: Approved
   For: 12 Against: 0 Abstain: 0

8. **Protocol Title:** 2007-38261A Bobcat and fisher habitat use and interactions
Species &Pain Class:(B) Fisher; (A,B) Bobcat; (A) Voles, mice, lemmngs; (A) Chipmunks, red squirrels, flying squirrels; (A) Shrews
Question the Research Addresses: PI requests 40 class B fishers; 34 class A and 35 class B bobcats; 4750 class A voles, mice, and lemmings; 440 class A chipmunks, red squirrels, and flying squirrels; and

600 class A shrews for a study to collect and summarize foundational data on bobcat and fisher habitat use, diets, and activity patterns to learn why female fishers are so vulnerable to being killed by bobcats. The specific goals are to deploy GPS collars on bobcats and fishers, monitor habitat use to identify areas where fishers are vulnerable to being killed by bobcats, describe seasonal diet composition and overlap between bobcats and fishers, characterize activity patterns of bobcats and fishers, investigate the role of forest management in bobcat and fisher population trends, and update our understanding of bobcat ecology in Minnesota.

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

Comment: I see that a permit for the trapping of adult fisher and bobcat has been attached. Is a permit to lethally trap all the pray species needed as well? Is a permit also needed for the handling and ear tagging of the bobcat kittens in the dens?

Comment: I might be missing it, but I don't see that an alternative search has been performed. Since you have animals in category B, please perform an alternative search as requested by this section. A sample template has been sent via email, please fill out and add to the protocol as an attachment.

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

9. **Protocol Title:** 2105-39123A Targeted Membrane Integrity in Cardiac Ischemia and Reperfusion
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: PI requests 55 class B pigs for a study to examine whether a copolymer membrane stabilizer, poloxamer 188 (P188), will promote mitochondrial viability and preserve myocardial function in a porcine model of ischemia/reperfusion.

   Committee Decision: Approved
   For: 12 Against: 0 Abstain: 0

10. **Protocol Title:** 2107-39284A Use of Inhaled Argon During Hemorrhagic Shock
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: PI requests 24 class B pigs for a study to examine whether use of inhaled argon will offer organ protection in a porcine model of hemorrhagic shock.

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

    Comment: Please add the cystocentesis and echocardiography procedures into the surgical hemorrhagic shock surgical procedure, or add them as separate procedures.

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

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 1)**

1. **Protocol Title:** 2001-37801A Development and Translation of an Intracranial Nerve Implant
Species &Pain Class:(B) Nonhuman Primate (Macaques)
Question the Research Addresses: PI requests permission to capture through microscope pictures of array placement, which will be used for grant reporting and publication, and to add a reversal for dexmedetomidine for shorter procedures.

   Committee Decision: Approved
   For: 12 Against: 0 Abstain: 0
   Member 15 out

Institutional Animal Care and Use
Committee 10/05/21 Minutes
VCRC - 76D

Meeting Convened: 12:00PM	Quorum Requirement: 9
Meeting Adjourned: 2:01PM	Members Present to Vote: 13

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v8.0** 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

1. A representative from the Veterinary School faculty presented a proposal for adjustments to the way in which veterinary teaching activities using client owned animals are managed by the IACUC. The request includes exempting teaching activities with client-owned animals from the normal IACUC review process. The committee discussed the proposal and noted that the IACUC needs to retain jurisdiction over these activities. The committee will reach out to peer institutions to examine their policies for veterinary teaching and will work with the vet school to determine a way to streamline the approval process and provide flexibility for clinical and staffing situations in teaching protocols, while retaining jurisdiction.
2. The committee was updated on a PI whose use of cats has been suspended. The committee will be in touch with the PI regarding next steps following a scheduled leadership meeting with anesthesiology consultants from the Veterinary Medical Center. The suspension of the PI's use of cats remains in place until further notice.
3. The committee was updated on ongoing health issues with hamsters and overall animal care in Duluth. IACUC leadership met with the Associate Dean there and have planned for regular meetings and additional training for Duluth animal care staff.
4. The committee discussed a self-report in which rats died in a hypoxia chamber due to potentially faulty equipment. The lab has contacted the manufacturer and taken steps to fix the chamber. The committee was satisfied with the corrective action plan and considers the matter closed.
5. The committee was informed of the current Chair's plan to step down starting in the new year. A new Chair will be needed and must be someone who has not been an IACUC Chair or Vice Chair in the past. It should be someone familiar with animal work at the University, the regulations surrounding such work and the operation of the IACUC committee.

1. **IACUC-R1S1(# Protocols: 15)**

    1. **IACUC-R1S1 - NEW(# Protocols: 12)**

        1. **Protocol Title:** 2106-39212A MN Artificial Insemination Class
           Species &Pain Class:(A) Cow (Agricultural)
           Question the Research Addresses: This is not a research protocol.

           Committee Decision: Approved
           For: 13 Against: 0 Abstain: 0

        2. **Protocol Title:** 2108-39354A Clinical Evaluation of a Novel Post-Polypectomy Perforation Prevention Device
           Species &Pain Class:(B) Pig (Biomedical)
           Question the Research Addresses: The objective of the study is to evaluate the biocompatibility and safety of ThermoGel for colonoscopic polyp removal in a swine gastrointestinal model. This is a suitable test system for evaluating the performance of a submucosal injection agent because the pig rectum and stomach is a practical and widely available animal model that most closely resembles human stomach and large intestine.

           Committee Decision: Approved
           For: 11 Against: 0 Abstain: 0
           Members 1 and 10 out

        3. **Protocol Title:** 2108-39325A In vivo optical imaging and characterization of cerebral physiology during tumorigenesis
           Secondary Reviewers: Fritz, Sabine and Greenberg, Kate

Species &Pain Class:(B,C) Mice
Question the Research Addresses: How does brain tumor growth disrupt normal brain function?

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

Comment: In the experimental design section, it is described that imaging sessions will be performed up to 21 days post-tumor induction, and that animals will be euthanized at the end of 21 days (or earlier). However, in the proposed timeline, tumor induction is estimated to occur at Day 17, with the experiment ending on day 41 (24 total days, including a 3 day recovery period post-tumor induction). Please clarify whether animals will be euthanized at 21 days post tumor-induction or 21 days after the recovery period (and 24 days after the actual induction procedure).

Comment: The imaging/electrophysiology sessions are described as lasting up to 6 hours, but it is stated that the animals will be removed from restraint if showing distress. Please indicate a typical session duration, and what signs of distress will be monitored.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

4. **Protocol Title:** 2107-39255A "Optical Imaging of Cerebellar and Cerebral Circuits in Normal and Disease Mouse Models"
Species &Pain Class:(A,C) Mice
Question the Research Addresses: The overall goals of this project are to understand the function of the cerebellar and cerebral cortical circuits, both in health and when these circuits are disrupted in various disorders. Calcium optical imaging of neuronal activity in awake, behaving mice, combined with electrophysiological and optogenetic tools, are used to study the functions and interactions between cerebellar and cerebral cortical circuits in normal and transgenic mice.

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

Comment: Your justification for the [redacted] space is that [redacted] does not have a reverse light cycle room, but this is no longer true. Please remove the [redacted] section from the protocol or update and clarify the justification within the [redacted] section.

Comment: Your attachments should be updated to reflect the current protocol. For example, the flowchart for experimental procedures and behavioral testing and mouse groups attachments still refer to protocol 1808-39255.

Comment: In the MR scanning procedure you say that mice will not be imaged more than once per day, but the Muscimol injection procedure contradicts this. Please explain why mice need to be woken up from anesthesia to then be anesthetized for the muscimol injection and then anesthetized again in an hour. It seems like this could be pared down to 1, or at least 2, anesthetic events.

Comment: Please provide a reference for adult mice drinking 2mls/day. The lowest reference I can find is 3mls, although most claim 4-6mls/day. This is important as it dictates the 50% water restriction you are requesting.

Comment: In the Viral Vector Injection surgery you mention administering the virus via RO injections, but I do not see this a procedure on the protocol. Please add RO injection as a procedure.

Comment: Please add Carprofen to the Prophylactic/Intra-procedureal Analgesic table, as you describe using it in addition to NeoPredef and Bupivicaine for the epileptic kainate mice.

Comment: Please include the rationale for water restriction, as opposed to other methods like food restriction or food/sugar rewards, within the protocol itself.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

5. **Protocol Title:** 2107-39289A Striatal plasticity in a rodent model of Parkinson's disease with progressive dopamine degeneration

Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: First the mitoPark mouse model will be characterized in our hands. We will assess the time course of neurodegeneration and behavioral symptoms associated with degeneration. Second, we will investigate the functional and anatomical adaptations, with or without chronic methamphetamine administration, of the principal neuronal type within the striatum, the spiny projection neurons, to determine what adaptations occur prior to the onset of motor symptoms and are thus hypothesized to be homeostatic and what adaptations occur at the onset and after motor symptoms arise and thus hypothesized to be pathological. Another question are trying to answer is we want to know if is if chronic methamphetamine is neurotoxic to and what impact chronic meth use and abstinence/withdrawal has on learning and learned behavior.

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

Comment: In the experimental design section, it is described that animals may receive a 15 minute pretreatment of methamphetamine at a dose of 2mg/kg or 5mg/kg IP. In this procedure description, a pretreatment dose of only 2mg/kg is listed. Please adjust one of the sections for consistency as to which pretreatment doses may be administered.

Comment: The last paragraph in the experimental design says "Therefore, a total of 64M and 64F, to check for sex differences, mice will be needed to complete Aim II." The preceding paragraph (titled "calcium permeable AMPA receptors") describes numbers needed for this section with a total of 256 mice. Please update the protocol to clarify the total number of animals that will be required for Aim II.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

6. **Protocol Title:** 2108-39309A IMHA Housing SOP Protocol for [redacted]
Species &Pain Class: (A) Mice
Question the Research Addresses: Specific research questions and aims will be addressed on the experimental protocols that reference this SOP.

The committee deferred this protocol to a subsequent full committee meeting.

Committee Decision: Deferred
For: 13 Against: 0 Abstain: 0

7. **Protocol Title:** 2108-39373A Tick Immune Signaling, Microbiota, and Acquisition of Borrelia burgdorferi and Anaplasma phagocytophilum
Species &Pain Class:(A,B) Hamster; (A) Mice
Question the Research Addresses: This is an NIH funded P01 project involving scientists at U MN, U MD and Yale. We will develop and operate a "Tick Core": The core will provide necessary research reagents to 3 other projects, including I. scapularis ticks, cell lines and tick cells modified via clustered regularly interspaced short palindromic repeats (CRISPR/Cas9 or reporter tags). The Core will also instruct personnel from all projects on how to cultivate, prepare, or manipulate tick cells and ticks.

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

Comment: The following apply to the Hamster IMHA responses: - In the IMHA section question 5 you state that [redacted] Is this true? Or is this simply the space that RAR visits because of animal housing/procedures? - For question 12, please note that RAR also offers species specific training upon request. The hamster course covers basic handling, restraint, sexing, and how to identify a sick vs. healthy hamster. - In question 13 you state that animals recovering from anesthesia are checked every 30 min, but I'm not sure what this means. Do you mean that you continue to check on them once they are full recovered from anesthesia? Animals should be monitored continuously until ambulatory and fully recovered from anesthesia per the IACUC Guideline on Anesthesia Monitoring of Research Animals. - For question 22, how is the rack sanitized and how often is it done? How are feed and bedding storage bins sanitized, and how frequently? How often are water bottles sanitized? - For question 27c, the RAR on-call pager number is 612-899-6285. You currently have the main RAR office number, which is not manned after hours or on holidays. - For question 31, please confirm that animals would still have access to fresh air supply in the case of a power outage. I am unfamiliar with what [redacted] has, which is why it should be listed in the protocol.

Comment: Please provide additional details on how you arrive at 10 breeders and 140 hamsters generated. How many pups do you have per litter? How many litters are generated per year? How many litters would a single female hamster deliver? How many of the breeders are females vs. males? You previously states that females are placed with 2-4 males, so I have to imagine that a good portion of your designated 10 breeders are male.

Comment: The following apply to the Mouse IMHA responses: - In the IMHA section question 5 you state that Rooms [redacted] but I do not think RAR owns this place. Please review and reconcile. - For question 12, please comment on how training occurs. Is it in person, or didactic? Does the trainer see cases side by side with the new employee? How are common rodent health conditions, in addition to study specific concerns, taught to new personnel? - Please select "yes" to question 18, as you then go on yo describe situations where mice will be housed individually. If male mice are ordered, they cannot be re-paired. This only need to be changed if you are actually placing ticks on mice. - For question 20, you state that mice are individually housed while ticks are placed, but everywhere else in the protocol you state that mice are needed to generate antisera. Mice undergo SQ injections at the base of the tail. Are you actually placing ticks on mice? - For question 22, how is the rack sanitized and how often is it done? How are feed and bedding storage bins sanitized, and how frequently? How often are water bottles sanitized? - For question 27c, the RAR on-call pager number is 612-899-6285. You currently have the main RAR office number, which is not manned after hours or on holidays. - For question 31, please confirm that animals would still have access to fresh air supply in the case of a power outage. I am unfamiliar with what [redacted] has, which is why it should be listed in the protocol.

Comment: For mice, you talk about the endpoint occurring after tick feeding. Again, elsewhere in the protocol you state that mice are only being used to generate antibodies. Are ticks being placed directly on mice?

Comment: Again, your responses to questions 1 and 3 for mice talk about placing ticks directly on mice, but this is not described in the Experimental Design and there is no associated procedure elsewhere in the protocol. The mouse section should talk about adverse health effects related to adjuvant use, such as swelling, erythema, discomfort, reaction/vocalization to being picked up by the tail, etc.

Comment: Is there a reason why ticks need to placed on the hamster's head? Is it because there is shorter hair along the face? If this is why, please explain why angora hamsters are the preferred breed, or provide a reference comparing standard golden and angora hamsters. Per RAR's website, eye lube should be used whenever the anesthetic event is >5 min. RAR also states that supplemental heat should be provided during all anesthetic events. Supplemental heat sources include circulating water blankets, air heating devices, or commercial products that can be heated up or create heat via a safe chemical reactions. NO electric heating pads are allowed for use with hamsters. The IACUC guidelines on Anesthesia Monitoring of Research Animals also covers this. Note that the hamsters should be monitored continuously while under anesthesia, and values should be documented every 15 minutes.

Comment: Please remove the following "The animals will be kept [redacted] y" as RAR does not maintain the facility and IACUC does not approve [redacted]; IBC should be approving the space as appropriate [redacted].

Comment: You attachments are out of date. The Mouse attachment references a protocol from 2016 and describes using 225 mice in two different aims, which doesn't reflect what you have written in the body of this protocol. The same is true for the hamster attachment; the numbers do not match. I recommend removing both attachments as they are not necessary and the relevant information is within the Experimental Design section of this protocol.

Comment: Your alternative search is 3 years old and needs to be updated. Specifically, I'd like your search to address any new data on infecting sub-adult ticks via the bovine membrane method as this appears to be a opportunity for replacement, which is one of the 3 Rs. As I understand it, this is the only reason hamsters are required and why you are unable to completely transition away from a mammalian model. I'd also like to see a search comparing animals models in general, and why hamsters are necessary compared to something like rats.

Comment: The procedure is titled "Infect ticks with Anaplasma and Borrelia" but you only describe administering anaplasma.

Comment: Are you really purchasing 10 hamsters from an external source, or are they being transferred from another protocol? Have you spoken with your RAR veterinarian on where securely source angora hamsters from?

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

8. **Protocol Title:** 2108-39327A CVM 6804 (VMED 5670): Food Animal Surgery and Anesthesia Rotation
Species &Pain Class:(B) Cow (Biomedical)
Question the Research Addresses: NA

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

Comment: Please provide dosing details for Lidocaine administration given for local anesthesia (and/or IV) in all procedures using Lidocaine as a local block.

Comment: The time lines in between the survival procedures and terminal procedures in the calves seem to be inconsistent. Could you provide clarity on the amount of time between the end of the survival procedure and then beginning of the terminal procedure?

Comment: If a tracheotomy is required during the procedure, will a repair be performed? Will this impact the ability to intubate during the terminal procedure?

Comment: Can you please provide more clarity on if Epinephrine and oxytocine will be used for the Csections? As I understand it, they are commonly used for field Csections, however, it would be more instructive for the students to see the uterine tone that results from withholding those medications? What are difficulties that can arise by performing a Csection without giving these medications.

Comment: Please provide the dose for euthanasia used in the terminal procedure.

Comment: Please update the procedures to include an analgesic regimen for post-operative pain management of cows and calves who have undergone surgery. Note that the analgesia plan should consist of 72 hours post-operative pain relief.

Comment: While it is understood that full anesthetic records are not kept for the standing surgeries, a record of the adequacy of the local anesthesia/sedation as well as any redosing that is needed, should be kept. Please update the procedures to confirm.

Comment: Please update the numbers justification to provide additional detail on the number of animals requested.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

9. **Protocol Title:** 2101-38780A Mermelstein Mouse Protocol Mechanisms and circuitry in mouse models of addiction Academic Investment Research Program (“AIRP”), Center for Neural Circuits in Addiction "Center for Neural Circuits in Addiction" NIDA P30 grant
Species &Pain Class:(B) Mice; (B) Mice
Question the Research Addresses: How do environmental manipulations, particularly drug exposure and subsequent withdrawal, alter the membrane parameters of the nucleus accumbens? How do these drug-induced changes mimic “natural” manipulations, like food restriction, novelty, or stress? What are the long- and short-term consequences for these changes on behavior?

Committee Decision: Approved
For: 13 Against: 0 Abstain: 0

10. **Protocol Title:** 2109-39415A Identifying the Molecular Mechanisms of Self-Renewal and Relapse in Human AML through Xenograft Mouse Models. Therapeutic vulnerabilities in acute myeloid leukemia stem cells with TP53 alterations.
Species &Pain Class:(A,C) Mice
Question the Research Addresses: We would like to determine whether the self-renewal transcriptional subgroups are associated with previously defined signaling states of normal hematpoietic precursers, and if if our murine single-cell transcriptional signature of self-renewal is also associated with self-renewal and relapse in Hu AML. In addition, we plan to determine the functional relevance of candidate signaling pathways by testing the effect of pathway inhibitors on global signaling states by perturbations of signaling pathways by using specific pathway inhibitors.

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

Comment: Please provide diluent for SL-401 and Elesclomol.

Comment: Please update Controlled Substances page by providing information about Ketamine.

Comment: Please update IBC page to reflect use of human cells and genetically modified mice.

Comment: If the tail vein is damaged during the first or second injection and can no longer be used, what route will be used to administer the subsequent injections?

Comment: You state the mice receiving inhibitor treatment will be sacrificed if severe cytopenias are detected and reference a platelet count of <100,000. If this is supposed to be 100,000 platelets/ul, this is definitely not severe thrombocytopenia. Please amend and provide your critical platelet number for euthanasia.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

11. **Protocol Title:** 2105-39089A Biodistributiion, Toxicity, and Tumorigenicity Evaluations; Preclinical Studies in Pluripotent Stem Cell-Derived Myogenic Progenitors to Enable a First-in-Human Phase 1 Safety/Dose Escalation Trial for Duchenne Muscular Dystrophy
Species &Pain Class:(B,C) Mice
Question the Research Addresses: Tissues collected from mice transplanted with different doses of myogenic progenitor cells over a range of both short and long term time points will be examined to discover the distribution or localization of transplanted cells, whether there are acute or chronic toxic effects from the transplants, and whether the transplanted cells are associated with increased risk of tumor formation.

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

Comment: Please update the protocol to provide a statement for monitoring animals recovering from anesthesia for both surgical procedures, particularly if deep anesthesia with ketamine/xylazine will be used.

Comment: Please describe in the health and monitoring, specific care for the surgical sites, especially since you are requesting that they be bilateral. Things to check would be use of limbs, dehiscence of the incision, and signs of infection (redness, swelling, discharge). Additionally, since you are requested an exemption for the use of analgesia, please also describe how you will monitor and rate possible lameness or disuse of the limbs and what endpoints would be given deficits. Things to monitor for would include ability to reach food and water, normal posture ability (e.g. rearing during exploration), and ability to create adequate nests with enrichment material.

Comment: It states in the third section of the health and monitoring that animals will be euthanized if they meet euthanasia criteria but it is not stated specifically what that criteria will be. There is a list of clinical signs listed in section 2 but it is not clear what will be done when they are noted and when action will be taken to euthanize or provide further care. Please further describe what the criteria is for euthanasia and make sure to add the surgical sites and the possible outcomes as part of the criteria.

Comment: It is noted that the injections of cardiotoxin will happen bilaterally. Many publications as well as the collaborator's lab use the contralateral leg as a control (no cardiotoxin). Given that analgesia will not be given, can you justify creating bilateral surgeries and muscle necrosis as this could lead to deficits of normal movement.

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

12. **Protocol Title:** 2108-39344A Preclinical Gene Therapies for Pediatric Disorders Next generation Genome Editing
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: Can we define and test novel gene therapeutics to ameliorate

tragic genetic disorders of childhood?

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

Comment: The electroporation surgery has the following description: Percentage of isoflurane during procedure may be in the range of 1%-5% dependent on respiratory rate and quality (~180 bpm undisturbed with an allowable 50% reduction while anesthetized). If the mouse is found to be light from anesthesia noted by movements, increased respiratory rate and/or response to toe pinch, isoflurane will be increased. If the mouse is found to be too deep from anesthesia as seen by decreased or shallow respiratory rate, the anesthesia will be decreased. Please clarify whether RR is monitored in the "parameters monitored" section, whether it applies to pentobarbitol as well, and whether it applies to the imaging procedure as well.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 3)**

1. **Protocol Title:** 2003-37989A Modulation and plasticity in respiratory motor control Targeting Estrogen Receptors to Restore Spinal Plasticity in Acute Spinal Cord Injury (MN SCI Grant) The Role of Spinal Estrogen Signaling for post-SCI Neuroplasticity (Craig H. Neilsen Foundation) Estrogen Receptor Signaling in the Expression of Respiratory Motor Plasticity
Species &Pain Class:(A,B) Rat
Question the Research Addresses: These studies are specifically designed to investigate sexual dimorphisms and the role of sex steroid hormones (examples: estrogen, progesterone, etc...) in the expression of respiratory neuroplasticity in naive rats and in the context of injury or obesity.

   Committee Decision: Approved
   For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 2003-37991A Adjuvanted Opioid Vaccine for Treating Fentanyl Use Disorder to Reduce Poisoning and Fatal Overdose
Species &Pain Class:(B) Pig (Biomedical); (B) Rabbit
Question the Research Addresses: The overall hypothesis is that a vaccine targeting fentanyl and its analogs (either as individual vaccines targeting either fentanyl or its analogs or as a a multivalent vaccine formulation consisting of co-administration of multiple conjugates) will offer selective but also broad protection against the fentanyl-like family. We have employed similar strategies against heroin, oxycodone, and nicotine.

   Committee Decision: Approved
   For: 13 Against: 0 Abstain: 0

3. **Protocol Title:** 2009-38418A Short term cardiovascular monitoring in the sheep: effect of renal denervation in hypertension
Species &Pain Class:(B) Sheep (Biomedical); (B) Pig (Biomedical)
Question the Research Addresses: This research works to address the mechanism and importance of the neural-cardiovascular-renal interaction in the development and maintenance of hypertension.

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

   Comment: Were all the sheep previously allotted for this protocol used on this experiment? If so, why now the move to pigs as the challenge with the rumen should have been discovered by the first surgery?

   Comment: Is the goal to entirely switch the model to swine? Should only a few swine be added as a pilot to ensure the swine model works? Should the remaining unused sheep (if any) be removed from the protocol?

   Comment: Please note that the corneal reflex should not be absent under anesthesia. A more appropriate reflex to check would be the palpebral reflex, which should be absent under an adequate plane of anesthesia.

Comment: Is there any reason these pigs would be housed at [redacted]? If not, please remove [redacted] language from the pig sections.

Comment: Current recommended dosage is Telazol 2-7 mg/kg + Xylazine 0.2-1 mg/kg. Propofol induction 2.5-3.5 mg/kg. If you have experience with the listed doses in the protocol that is fine (higher sedatives and lower induction). If not, suggest altering to RAR's current guidelines.

Comment: You don't really give the reason why you need to perform the experiment bilaterally. Can you please provide information about why unilateral renal manipulation did not work?

Comment: Are there any additional health implications associated with performing the experiment bilaterally? Please update the Health and Monitoring section accordingly.

Committee Decision: Stipulations must be met
For: 11 Against: 0 Abstain: 0
Members 1 and 10 out

Institutional Animal Care and Use Committee
10/12/21 Minutes
VCRC - 76D

Meeting Convened: 12:00 PM	Quorum Requirement: 9
Meeting Adjourned: 12:10 PM	Members Present to Vote: 13

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	X	(O, U)

Institutional Veterinarian:

3	X	(M, V)

Correlates to Version **v8.0** 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

1. The committee discussed a lab's history of adverse events, self-reports, and cooperation with RAR and the IACUC committee. The committee unanimously agreed and approved to close the current cat protocol and require the lab to submit a new cat protocol with limits on number of cats, procedures, and potentially age. The committee will also require the lab to have VMC anesthesiologists supervise anesthetic events until the anesthesiologists and the committee are ready to allow the lab to be independent.

1. IACUC-NEW (# Protocols: 0)

2. IACUC-AMENDMENT (# Protocols: 0)

Institutional Animal Care and Use Committee Minutes

VCRC - 76D

Meeting Convened: 12:00PM	Quorum Requirement: 9
Meeting Adjourned: 1:16PM	Members Present to Vote: 14

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V) Alternate

Correlates to Version **v8.0** 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

1. The committee was updated on the 2021 September inspection summary.

2. The committee was updated on a PI whose use of cats has been suspended and cat protocol has been closed. The PI will work with veterinary anesthesiologists to develop best anesthesia practices and will submit a limited scope protocol for committee review. No work with cats will be able to resume until the new protocol has been approved.

3. A request to change the committee's management of veterinary teaching protocols using client-owned animals was tabled to wait for an update on how these policies are managed at a peer institution.

4. The committee discussed a self-report in which a study using cows housed on an Agricultural SOP was initiated prior to having an approved research protocol in place. Project work has ceased until IACUC protocol approval is granted. The committee feels that the PI now understands the importance of receiving approval before beginning a study. The committee considers the matter closed.

IACUC-R1S1(# Protocols: 9)

1. **IACUC-R1S1 - NEW(# Protocols: 7)**

    1. **Protocol Title:** 2105-39112A IGF system in pain
    Species &Pain Class:(A,B,C) Mice; (A,C) Rat
    Question the Research Addresses: How does IGF1, IGF2, and IGF1r regulate pain? Can we find novel compounds to mitigate pain through IGF signaling pathway?

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

    Comment: In aims 2 and 3A, it is stated the mice will undergo multiple behavior tests. Please update the protocol to describe the amount of rest time each animal will be given between each of the behavior tests.

    Committee Decision: Stipulations must be met
    For: 14 Against: 0 Abstain: 0

    2. **Protocol Title:** 2108-39351A Evaluation of an automatic delivery system for an antidote to acute cyanide poisoning.
    Species &Pain Class:(B) Pig (Biomedical)
    Question the Research Addresses: The purpose of this study is to evaluate the performance and efficacy of the novel automatic delivery system in administering sulfanegen to a large animal model.

    Committee Decision: Approved as submitted
    For: 12 Against: 0 Abstain: 0
    Members 1 and 10 out

    3. **Protocol Title:** 2106-39180A Immunopathology and adverse fetal outcomes after maternal cytomegalovirus infection T cells and cytomegalovirus-associated immunopathology
    Species &Pain Class:(A,C) Guinea Pig
    Question the Research Addresses: How does cytomegalovirus infect the placenta? How does the host immune response to either placental or fetal infection cause adverse pregnancy outcomes? How is the fetal immune system affected by prenatal exposure to CMV?

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

Comment: In the experimental design, all blood collection procedures are described as occurring by toenail clip. However, in this procedure, the ~65 day period weekly sampling is described as occurring from the ear vein. Please clarify if ear vein sampling is expected to occur.

Comment: In the experimental design, AMG487 or vehicle administration is described as being repeated only every 48 hours. In the procedure for AMG-487 treatment, administration is described as able to occur either every 24 or 48 hours. Please adjust the description in the experimental design to align with this 24-48 hour repeating administration.

Comment: Toenail clipping is a painful procedure that is being phased out of modern blood collection techniques. The Army protocol cited from 2007 cites using local anesthetic to numb the toe prior to collection. No anesthetic is mentioned in your protocol. Please consider revising your peripheral blood collection technique or adding a local anesthetic.

Comment: One of the stated endpoints in the procedures is to euthanize the L2C guinea pigs if their WBC is over 300,000/mm3 or exhibiting poor clinical signs. Please provide the time-point for the L2C guinea pigs in this section.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0
Member 4 out

4. **Protocol Title:** 2108-39365A Multi-Compartment Tool for Endoscopic Fine Needle Aspiration
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: There is a need for a multi-compartment fine needle aspiration device that can simplify the FNA procedure allowing for efficiency and less distraction for the operator and assistants. This research proposal will evaluate a newly designed tool for the FNA procedure.

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

   Comment: Will the animal be disconnected from the ventilator during the bronchoscopy? If so, how will you adequately ventilate the animal? It is possible that the pig could be apneic during this transition. It is mentioned being ready to support ventilation but it is not clearly defined in the procedure section. I would suggest that the pig be weaned from the ventilator and be spontaneously breathing before the device is inserted into the tracheal tube. If O2 saturations fall below 90%, the device should be removed animal should receive oxygen and assisted ventilation until staturations improve. Or, Will a double lumen endotracheal tube be used to facilitate ventilation and bronchoscopy? Please update the protocol to clarify.

   Comment: I would include a euthanasia step in the procedure description which includes the method of euthanasia and drug information including the dose.

   Committee Decision: Stipulations must be met
   For: 14 Against: 0 Abstain: 0

5. **Protocol Title:** 2108-39348A Prostate Cancer Studies-eIF4A-HK2
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: To test the hypothesis that inhibition of HK2-mediated Warburg effect by targeting eIF4A1-dependent HK2 mRNA translation axis prevents CRPC development.

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

   Comment: Is it correct that animals will receive an IP injection every day for 18 weeks? Is there precedent for this? Please justify in the context of other potential methods (i.e. osmotic pumps or pellets that might require much less stressful handling). Please update the protocol to include the justification and any precedent.

   Comment: Please work with your area vet to develop a clinical scoring system or other criteria that can be used to

identify animals that are approaching endpoint. Animals meeting these identified criteria should be monitored at least two times per day. Please update the Health and Monitoring system to include the monitoring plan as discussed with your vet.

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

6. **Protocol Title:** 2108-39309A IMHA Housing SOP Protocol for [redacted]
Species &Pain Class: (A) Mice
Question the Research Addresses: Specific research questions and aims will be addressed on the experimental protocols that reference this SOP.

   The committee deferred this protocol to a subsequent full committee meeting.

   Committee Decision: Deferred
   For: 14 Against: 0 Abstain: 0

7. **Protocol Title:** 2109-39391A Mouse models to study cancer progression and resistance to therapeutic interventions Center for Modeling Tumor Cell Migration Mechanics: (Project 2) Cell Migration in Mechanically Complex Microenvironments Re-engineering the stroma to enhance anti-tumor immunity and immune therapies Stromal re-engineering to enhance anti-tumor immunity and immune therapies A platform to functionally sort and analyze tumor cells within combinatorial metastatic micorenvironments Stromal re-engineering to promote responsiveness to checkpoint blockade Integrated Immune Engineering for Poor Prognosis Cancers Center for Multiparametric Imaging of Tumor Immune Microenvironments
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: We aim to elucidate the physical and molecular mechanism by which cancerous cells interact with their local microenvironment to invade adjacent tissue and metastasize and how these features impede therapeutic interventions, and develop novel therapeutic strategies to combat human cancer.

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

   Comment: The Breeding procedure is currently listed as class C presumably to account for the mice that will develop cancer due to their genotype and may become moribund, but it appears that not all mice generated by breeding will actually fall into class C. Please create a separate Tumor Induction procedure for genetically-based tumors, making this new procedure class C and changing the Breeding procedure to class A.

   Comment: Please include the mg/kg dosage of enrofloxacin that will be provided for mice with signs of infection. Recommend contacting RAR if signs of infection are noted to determine a treatment plan, however, if wish to include in your protocol, recommend using dosage of 10mg/kg SQ once daily. Have you had issues with infection in the past that antibiotic therapy needs to be included? If so, recommend reaching out to your area veterinarian to discuss this issue as infections should not occur at a high rate and are likely confounding variables to your study goals. Suggestions can likely be made to improve success rate and avoid need for antibiotics + additional stress to mice for daily injections.

   Comment: For the question within the Anesthetic Regimen section, "What specific steps will be taken in case any of the measured values are outside acceptable ranges?" please also include that if the mouse is found to be too deep from anesthesia, noted by decreased respiratory rate and shallow breaths the isoflurane level will be decreased.

   Comment: Please include that heat support will be provided to the mice while anesthetized until recovered.

   Comment: Please include that heat support will be provided to the mice while anesthetized until recovered.

   Comment: Please include additional details for the intracardiac injection technique including further description of how the injection is performed, needle sizes used and volume injected. Additionally, please include if any adverse events are seen (for example abnormal breathing or hemorrhage, the mouse will be euthanized.

   Comment: For mice on tumor studies, recommend including in addition to the % body weight loss as an endpoint also including if mice reach a body condition score <2/5 they will be euthanized. For mice with tumors or ascites,

body condition score can be a better indicator of weight loss as tumors and ascites can increase the weight of the mouse.

Comment: Please also describe the monitoring of the parabiosis mice within the Health and Monitoring section. Please include the information described in the procedure (daily checks 7 days following surgery). And please include additional information for when these mice will be euthanized: dehiscence of surgical site, signs of infection (swelling, inflammation) at surgical site and if either one of the mice shows signs of lethargy, hunched posture, body condition score <2/5 both mice will be euthanized or RAR veterinary staff consulted.

Comment: Please create a procedure that lists all substances/ treatments described in the experimental design section that will be injected into the mice including the route, dosage and frequency. These include caerulein, losartin, halofuginone, relaxin, collagenase, ROCK inhibitors, FAK inhibitors, Plerifxafor, antifibrotics, all chemotherapeutics, all immunotherapies, etc

Committee Decision: Stipulations must be met
For: 14 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 2)**

1. **Protocol Title:** 1811-36490A Vaccines for fentanyl and its analogs: a strategy to reduce illicit use and overdose
Species &Pain Class:(B,C) Rat; (A,B) Mice
Question the Research Addresses: The overall hypothesis is that a vaccine targeting fentanyl and its analogs (either as individual vaccines targeting either fentanyl or its analogs or as a a multivalent vaccine formulation consisting of co-administration of multiple conjugates) will offer selective but also broad protection against the fentanyl-like family. We have employed similar strategies against heroin, oxycodone, and nicotine.

   Committee Decision: Approved
   For: 14 Against: 0 Abstain: 0

2. **Protocol Title:** 1909-37384A 1. Synaptic transmission and plasticity in the developing brain and neurological disorders 2. Aberrant neuronal excitability of the cerebellum in mouse models of autism spectrum disorder 3.Cerebellar underpinnings of anxiety/depression-like behaviors in a social isolation mouse model 4. Effects of social isolation embedded in the cerebellum of mouse models for autism spectrum disorder 5. Distinct psychiatric-relevant behaviors are modulated by the ventrolateral thalamus or ventral tegmental area connected with the cerebellum
Species &Pain Class:(A,B) Mice
Question the Research Addresses: To better understand brain development and several prevalent neurological disorders, we investigate the molecular basis that underlies synaptic transmission and plasticity.

   Committee Decision: Approved
   For: 14 Against: 0 Abstain: 0

University of Minnesota
Panel: FCR Panel
MINUTES OF MEETING
November 16, 2021
VCRC - 76D

Meeting Convened: 12:01PM	Quorum Requirement: 9
Meeting Adjourned: 1:18PM	Members Present to Vote: 11

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v8.0** 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

1. The committee voted unanimously to approve the Fall 2021 Semiannual Program Review document and send it to the Institutional Official.
2. The committee discussed a lab's plan to address a suggestion for improvement identified in the last AAALAC site visit. The lab had behavioral equipment that was not sanitizable. They have replaced non-sanitizable maze components with vinyl flooring and acrylic surfaces, and a sample maze has been observed by committee representatives. The committee endorses the plan to update all mazes with the new materials and requests an estimated timeframe for completion.
3. The committee discussed a subcommittee's recommendations on defining "wildlife" for purposes of reporting to USDA. More information will be gathered by the subcommittee on how to define "handling" for purposes of determining whether animals should be considered USDA-covered.
4. The committee discussed a self-report in which a rabbit received an injection via the intramuscular route, which was not approved on the protocol. Moving forward, the lab and RAR will both ensure that the procedures are checked against the approved protocol before being conducted. The committee considers the matter closed.
5. RAR notified the committee of recent difficulties obtaining standard buprenorphine and will update the committee if there is a need to change to a compounded formulation due to availability.
6. The committee Chair has requested information from a peer institution on their management of teaching using client-owned animals. In the absence of a response, the committee will proceed with developing their own policy.

IACUC-R1S1(# Protocols: 10)

1. **IACUC-R1S1 - NEW(# Protocols: 6)**

1. **Protocol Title:** 2110-39472A Evaluation of a novel gel to prevent adhesions
   Species &Pain Class:(B) Rat
   Question the Research Addresses: The question being addressed is how to prevent these post-operative abdominal adhesions by administering an effective preventative agent at the time of operation. Specifically, this study will continue to explore administration of a novel gel for this purpose.

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

   Comment: In the study design section please clarify that the acute group, n=10, is a non-survival group used for surgical practice. Acute and chronic is not defined in this section.

   Comment: I understand this is a pilot study for your project and you may not know your estimated effect size for a power analysis. Please further explain or cite related studies to support your experimental group sample sizes (n=10, n=5).

   Comment: Through out this section it is stated a few times that certain aspects of the study groups and numbers will be documented via protocol amendment. Please confirm that no experimentation on the animals that deviates from what is written in this protocol will be performed until such amendment has been approved by the IACUC, as amendments need to be approved before any modification to the study occurs.

   Comment: It is stated in the surgery procedure "Acute animals may not receive analgesics prior to their surgical procedure." It is doubled down in the acute study procedure. I am concerned that this statement implies no intra-operative analgesic effect and that these rats will experience pain during the surgery even though it is non-survival. Please clarify on your analgesic management for this group and whether any pain may occur during the acute surgery.

   Comment: For the dehisence procedure you mention using an EMLA cream. Please provide the included medications within the cream, dosage, route of administration, and duration of frequency for this product.

   Comment: In the attached study design it states "Volume of the experimental gel will be determined by concentration of active ingredient, to be determined." Please clarify what gels you are using in this experiment and what active ingredient is thought to be causing a beneficial effect.

   Comment: In the attachment for the chronic surgery it is stated that rats might be kept on a heating pad for 7 days post

surgery. Is this correct or did the PI intend to say that they would be on the heating pad for a few hours until recovered from the surgery?

Comment: Please describe the specific clinical signs you are monitoring for in your animals post op (ie increased respiratory effort/rate, hunched body posture, weight loss, etc).

Comment: "Identify and explain the rationale for the specific endpoint(s) for each animal or group of animals used in this protocol" please provide extra reasoning in this section for why the rats are staying for up to 30 days. Please identify other endpoints that you have accounted for with your 10 extra rats (unexpected euthanasia due to surgical complications or death) and provide detailed parameters (20% weight loss, etc).

Committee Decision: Stipulations must be met
For: 10 Against: 0 Abstain: 0
Member 1 out

2. **Protocol Title:** 2109-39454A Transcriptional regulation of myogenic stem cells
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: During development or following injury, what factors activate the stem cells in the skeletal muscles to allow them to divide and differentiate into mature muscle cells. An additional hypothesis is that dystrophin is an important factor and contributor in heart failure.

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

Comment: Based on the description, particularly the statement “We are transferring 615 mice from our old protocol”, it looks like that this protocol is for 3 year renewal. If it is for 3 year renewal, the PI needs to provide a brief summary of the research results from animals obtained during the prior approval period.

Comment: In this section there is nothing added to question e regarding what had been accomplished in the last three year approval period for this protocol. Assuming this is not a completely new protocol given the transfer of animals, etc. from the other sections of the protocol, please update this accordingly.

Comment: For Procedure 1 - The injection volume of 100ul is too large to inject into the muscles of the lower limb. Less than <50ul should be used and given the small size of these muscle groups an even smaller volume should be considered. In particular giving too much volume could lead to cardiotoxin not staying in the muscle where it is intended and also damage to the muscle from fluid pressure that could skew results.

Comment: Please expand on how group sizes were determined for procedures were harvesting stem cells is not the goal. Additionally, while the number of stem cells needed is stated, there is no calculation for animal numbers based on how many cells can be harvested per mouse. Please update the Justification of numbers to include calculations for group sizes based on statistical analysis where applicable as well as more detailed explanation for the number of animals needed for harvesting the needed number of myogenic stem cells

Comment: In this procedure it states that BRDU will be provided by water bottle. Please add a Food/Fluid restriction procedure and add the required information in that procedure.

Comment: Please add a Food/Fluid Modification procedure to outline the change in fluid availability requested in that specific procedure.

Comment: The PI described tail snipping for mouse genotyping. However, the PI does not describe the methods for mouse labeling. The methods for mouse labeling (such as ear tag, ear punch, among others) should be described.

Comment: In regard to Euthanasia Methods, are these the only 2 that are used on the protocol? For retired breeders and other mice that need euthanasia, CO2 euthanasia is a method that requires less specialized training in awake cervical dislocation. Please add CO2 euthanasia to this section (cervical dislocation as a secondary method after CO2 is encouraged). How are staff trained to provide awake cervical dislocation euthanasia?

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

3. **Protocol Title:** 2108-39309A IMHA Housing SOP Protocol for [redacted]
Species &Pain Class:(A) Mice

Question the Research Addresses: Specific research questions and aims will be addressed on the experimental protocols that reference this SOP.

Committee Decision: Approved as submitted
For: 11 Against: 0 Abstain: 0

4. **Protocol Title:** 2110-39484A Glial cell pathophysiology in glaucoma
Species &Pain Class:(A,B) Mice
Question the Research Addresses: 1) Does elevated intraocular pressure affect Ca2+ signaling in retinal Müller glial cells? 2) Does ocular hypertension affect structural interactions between Müller glia and retinal ganglion cells? 3) Does elevated intraocular pressure disrupt glutamate signaling in the retina?

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

Comment: Please summarize animal numbers to tie all of the pieces of information provided together. The Breeding procedure has justification for 600 animals, the Species section asks for only 460, and the Experiment Design section lists only the mice used in experiments. I think he really needs 600 mice, most of them in Pain Class A for breeding, to get the number of experimental animals needed to do the experiments, he just needs to spell it out.

Comment: The statistical box justifies 150 mice for the experiments; please justify the need for 460 mice.

Comment: Thank you for the detailed clarifications provided for the Experimental Design Section. Please update the experiment design section in the protocol with the information given in your response to reviewer comments. Also please update the Experimental Design section with the responses you provided about timelines around Tamoxifen injections in response to a comment about that procedure.

Comment: Please update this procedure in the protocol with the information provided in response to comments regarding details of the method for using the bell jar as an isoflurane induction chamber and for frequency of monitoring to provide adequate analgesia following the procedure. These same 2 details should be included in the procedure for microbead occlusion injection as well.

Comment: Please add to the procedure the methods that will be used for disinfection and control of bleeding in the tail snip procedure.

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

5. **Protocol Title:** 2108-39371A Efficacy and Toxicity of Human CD19-Specific CAR T-Cells
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: How do CD19-specific CAR T-cells (called CART19 cells) cause cytokine release syndrome and neurotoxicity in a mouse model?

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

Comment: In the excel sheet with the numbers of mice for the outlined experiments, there are broken links (#REF!) in the "Complete Summary of Mouse Usage" The numbers of mice in the "Experimental-Summary" sheet do not match the numbers in the Species section of the protocol. Please correct this.

Comment: Please update the name of the excel sheet referenced at the beginning of the experimental design section. It is currently listed as "1807-36119A_Continuing_Review" instead of [redacted]_2108_39371A"

Comment: Acknowledgement was affirmed to the cycle 1 comment pasted below, but the corresponding change has not yet been made to the protocol. Please edit accordingly. "For the question about what steps will be taken if values are outside acceptable ranges, it says "If the values are below the range, we will immediately remove the isofluorane and allow the mouse to recover." If values are low, you can just decrease the isoflurane concentration until the mouse is stable, then continue the procedure. It's not necessary to immediately remove isoflurane."

Committee Decision: Stipulations must be met

For: 11 Against: 0 Abstain: 0

6. **Protocol Title:** 2012-38696A US-UK Collab: Drivers of diversity and transmission of co-circulating viral lineages in host meta-populations
Species &Pain Class:(B) Pig (Agricultural)
Question the Research Addresses: How does partial immunity to different strains of Porcine Reproductive and Respiratory virus (PRRSV) influence evolution of PRRSV in pig populations?

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

   Comment: Please clarify if the pigs for each successive passage group will be held in a separate room ie., away from the existing passage group? If not, indicated how the testing, vaccination, etc will be accomplished.

   Comment: The time of PRRS inoculation is inconsistent between the experimental design heading (45-120 days post vaccination) vs. the procedures section (28-60 days). Please reconcile this discrepency.

   Comment: You mention that for PRRS inoculation fractious pigs may be sedated, however no sedatives, dosages and routes of administration are listed. Even if RAR would administer the drugs, they should be listed in the protocol since they would be used for an experimental purpose.

   Comment: For Question 2 (you mention this elsewhere), add 2/x per day monitoring of animals showing progressive disease

   Comment: For Question 3, add BCS for consideration for euthanasia (would also indicate lack of feed/water intake and morbidity).

   Comment: Please review "IACUC Policy: Photography, Video and Audio Recording of Animals Used in Research and Teaching" and "Guidelines: Photography, Video and Audio Recording of Animals Use in Research and Teaching" and be aware that images collected may be subject to FOIA requests. https://research.umn.edu/units/iacuc/policies-guidelines/animal-use-guidelines-exceptions

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

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 4)**

1. **Protocol Title:** 2105-39105A Porcine Dosing and Imaging Study for Cardiac Adhesions
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: This study will explore the effectiveness of the test therapy in various dosages in preventing adhesions following cardiac surgery, in comparison to clinically available products.

   Committee Decision: Approved as submitted
   For: 10 Against: 0 Abstain: 0
   Member 1 out

2. **Protocol Title:** 1912-37717A Molecular dysfunction in corticolimbic circuits in mouse models of neurodevelopmental disorders
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: How are molecular and connectivity mechanisms in corticolimbic circuits recruited during goal directed behavior and executive function tasks, and how do these go awry in conditions associated with neurodevelopmental disorder, such as autism-linked genotypes?

   Committee Decision: Approved as submitted
   For: 11 Against: 0 Abstain: 0

3. **Protocol Title:** 1812-36615A Novel vaccination strategy for cancer prevention and treatment
Species &Pain Class:(A,B) Mice
Question the Research Addresses: The main question this research will address is whether the conserved UV-target genes can serve as novel cancer-associated antigens for developing next-generation cancer vaccines for prevention and/or treatment of UV-induced skin tumors.

Committee Decision: Approved as submitted
For: 11 Against: 0 Abstain: 0

4. **Protocol Title:** 2103-38926A Quantifying behavioral syndromes and the effects of environmental pollutants in small mammals along an urbanization gradient
Species &Pain Class:(A) Rodent (Other - Non-USDA)
Question the Research Addresses: This study intends to test whether urban environments will select for a correlated suite of behavioral traits (i.e. an urban behavioral syndrome") in populations of small mammals, facilitating their adaptation to these novel environments and the stressors they present. Further, we want to determine whether there is evidence that these animals are exposed to microplastics and the toxins associated with them, and if the physiological consequences of this exposure could disrupt the behavioral mechanisms enabling adaptation.

   Committee Decision: Approved as submitted
   For: 11 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee

11/30/21 Minutes

VCRC - 76D

Meeting Convened: 12:01PM	Quorum Requirement: 9
Meeting Adjourned: 1:23PM	Members Present to Vote: 13

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v8.0** 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

1. The committee was updated on the October 2021 inspection summary.

2. The committee discussed a request by a PI for a modification to an existing laboratory supervision plan. The committee is comfortable with current staff member running anesthetic events and voted to allow [redacted] to run anesthesia independent of supervision by an RAR veterinarian. The PI was notified that the existing supervision plan remains in effect unless additional changes are requested and approved by the committee.

3. The committee discussed a self-report in which a daily check of mice was missed in an investigator managed housing space. No animal welfare concerns were identified, and lab staff have been retrained on required daily check procedures. The committee considers the matter closed.

4. The committee discussed a self-report in which a surgical procedure was performed on mice under the wrong protocol. The procedure was performed in accordance with the protocol on which it is approved. Going forward, lab staff will check cage cards carefully before performing surgery. The committee considers the matter closed.

5. The committee discussed a self-report in which an anti-coagulation therapy different from the one approved on the protocol was used in sheep. No animal welfare concerns were identified. The lab has obtained a veterinary recommendation and subsequently submitted a protocol amendment. The committee considers the matter closed.

6. The committee discussed a report of an adverse event in which dogs developed unexpected medial patellar luxation following experimental arthrotomy surgery. The PI has worked with RAR veterinary staff to manage this complication while supporting the welfare of the animals, including provision of analgesics as needed. The committee considers the matter closed.

7. The committee discussed a report of an adverse event in which mouse pups were found alive in a garbage receptacle and subsequently euthanized. It was not possible to assign responsibility for this event, but lab staff in the area have been reminded not to remove nesting material from cages, in case animals become inadvertently entangled. The committee considers the matter closed.

8. The committee discussed a report of an adverse event in which rat pups were found alive in a bedding recycling receptacle and subsequently euthanized. It was noted that there have not been recent changes in nesting materials that might account for this event, or the event listed above (item 7). RAR husbandry staff are being retrained on cage change out procedures to ensure all animals are accounted for. The committee considers the matter closed.

1. **IACUC-R1S1(# Protocols: 10)**

    1. **IACUC-R1S1 - NEW(# Protocols: 8)**

    1. **Protocol Title:** 2110-39520A Acute evaluation of updated extracorporeal circuit components.
    Species &Pain Class:(B) Pig (Biomedical)
    Question the Research Addresses: The purpose of this study is to evaluate the replacement of old components with better more efficient ones (heater/cooler and heat exchanger) in a swine model of extracorporeal circulation.

    Committee Decision: Approved as submitted
    For: 13 Against: 0 Abstain: 0

    2. **Protocol Title:** 2110-39525A Evaluating a Pig Model of Pancreatic Cancer
    Species &Pain Class:(B) Pig (Biomedical)
    Question the Research Addresses: Transgenic miniature pigs expressing human pancreatic cancer mutations (one mutant allele of TP53, as well as Cre-inducible mutant KRAS) will be produced by our collaborators from Precigen Exemplar. To activate these mutations, we will inject a special Adenovirus encoding Cre recombinase (Ad5/3-Cre) to the swine pancreas.

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

    Comment: For Question 2, please consider adding some clinical signs that would be indicative of the pancreatic cancer

advancement or of growth of the other tumors you mentioned that might develop in Question 1.

Comment: The surgery lists acceptable vitals ranges, and then makes the statement that these ranges "will be superseded" on an individual basis. That means that these are not really acceptable ranges, which is what is asked for. It also refers to a baseline, whose measurement is not elaborated upon. The protocol also refers to the possibility of supplementing iso anesthesia with IV anesthesia. Please specify the drug (propofol?) and dosages in the agents in combination section. Also will this be done when increasing iso to 4% does not have the desired effect?

Comment: This procedure refers to "paralytics being administered". Please clarify.

Comment: This is non-invasive and not a surgical procedure, yet the procedure type is listed as surgery. Also please verify that all the physiological parameters specified can be readily monitored during a MR scan. (For example, is pupil location monitored while the animal is in the scanner?) Consider moving the info to an "other" procedure type for clarity.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

3. **Protocol Title:** 2110-39538A Viral Env immunogens
Species &Pain Class:(A,B) Mice; (B) Rabbit
Question the Research Addresses: What is the optimal immunogen (a substance that induces an immune response) to elicit broadly neutralizing antibodies against Env of HIV-1, SARS-CoV-2, and other viruses?

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

Comment: While the Experimental Design section highlights what study groups you'll use for "B" (the COVID-19 research) it isn't entirely clear what happens to the mice. How many injections will they receive? Which route? With how much time in-between? Is it exactly the same booster schedule as the HIV mice in "A"? The same is true for the level of detail in "C" -- what exactly happens to the mice? I also do not understand how the last 300 rabbits are being used. How is work performed in mice informing your decision on what to do in these rabbits? Perhaps the section can be re-organized so that rabbit work and mouse work are separated? It looks like this is what you tried to do originally but perhaps with amendments the "flow" of the design section was altered?

Comment: There is a procedure for intravaginal inoculation of HIV, but the Experimental Design section only comments on IV injection. Please add this to the Experimental Design section and confirm that mice are infected either route, but not both.

Comment: Is additional monitoring happening for the HIV challenged mice? In the procedure sections it sounds like mice will be monitored daily. Are there additional symptoms to monitor for in these animals? If mice will be kept for up to 1 yrs, is there a reason why they only need to be monitoring daily for the first 2 weeks?

Comment: Please update the dates on your lit search -- right now the search range goes to 2019 but it should go to 2021.

Comment: Please add ketamine as a controlled substance.

Comment: I do not see a strong justification for animal numbers. Even in pilot studies there should be some justification of numbers particularly for the rabbits.

Comment: How did you arrive at 5 animals/group?

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

4. **Protocol Title:** 2110-39503A Understanding the molecular mechanisms of lung cancer and vascular function
Species &Pain Class:(A,B,C) Mice
Question the Research Addresses: We hypothesize abrogation of DARPP-32 or t-DARPP expression in tumor cells and activation D2R signaling in endothelial cells can inhibit cancer cell drug resistance and angiogenesis, respectively, and improve the clinical outcome of lung cancer patients. We also hypothesize that VEGF and other permeability inducing factors (i.e. IL-6, eotaxin) mediate vascular permeability through STAT3, and thus, targeting this signaling cascade represents a promising strategy to reduce cancer progression, tumor metastasis, and the tissue damage associated with

permeability during cardiovascular disease.

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

Comment: Please update the protocol to address the discrepancy between the number of mice to be produced in house that is listed in the Mouse Species Table (11,901) and the number listed in the In House Breeding Procedure (2,280).

Comment: This procedure and the two listed subsequently (Injections of Lung Cancer Cells and Orthotopic injection of lung cancer with anesthesia) all appear to refer to the same procedure. Is it possible that this procedure is meant to be a description of subcutaneous implantation of tumor cells and the two subsequent protocols refer to orthotopic implantation? The latter two procedures can still be combined into a single procedure tab.

Comment: Moribundity is proposed as the endpoint for Protocol XIX, #5. Once a day monitoring is proposed to ensure that animals so not expire as a result of ling injury induced by LPS. Since animals can deteriorate quickly, animals may suffer for an inordinate time between checks. Please increase the number of daily checks to at least twice daily and update the protocol accordingly.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

5. **Protocol Title:** 2110-39521A Vaccines for fentanyl and its analogs: a strategy to reduce illicit use and overdose
Species &Pain Class:(B,C) Rat; (A,B) Mice
Question the Research Addresses: The overall hypothesis is that a vaccine targeting fentanyl and its analogs (either as individual vaccines targeting either fentanyl or its analogs or as a a multivalent vaccine formulation consisting of co-administration of multiple conjugates) will offer selective but also broad protection against the fentanyl-like family. We have employed similar strategies against heroin, oxycodone, and nicotine.

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

   Comment: Aim 1 - please update the protocol to define CpG and TLR and provide the names of the TLR agonists and comment on the expected effects and safety.

   Comment: Aim 1 - on the test days are the escalating doses delivered by a pump via a cannula or by s.c. injection every 15 or 17 minutes? If the latter, what is the max number of injections an animal might receive in a single test day? In the studies where full cumulative dose response studies are performed on up to 4 days 48 hours apart, what is the max number of injections a single animal might receive over the 8 day testing period? Please update the protocol to clarify.

   Comment: In Aim 1e, how will anesthetic depth be measured? It is noted that respiration, heart rate, pulse and O2 will be checked every 10 minutes but the objective is to determine if the vaccine interferes with depth of anesthesia. Therefore, a measure of anesthetic depth is needed (e.g. loss of righting reflex, toe pinch?), please update the protocol to include this.

   Comment: Aim 1B) What is gCAMP ? What is STING? Please update the protocol to provide 1-2 sentences on what these compounds are, their safety and what effects they are expected to produce, especially acutely.

   Committee Decision: Stipulations must be met
   For: 13 Against: 0 Abstain: 0

6. **Protocol Title:** 2109-39424A Nucleus accumbens fast-spiking interneurons regulate opioid reward and addiction; Dopaminergic modulation of nucleus accumbens during prospective and retrospective neuroeconomic decision making; Molecular Basis for Structural and Behavioral Effects of Chronic Opioid Exposure; Dysfunctional State Representations in Psychosis: From Neurophysiology to Neuroplasticity-based Treatment; Modulation of social behavior by mu opioid receptors in the nucleus accumbens; Exploiting endogenous opioids to selectively modulate accumbal synaptic transmission; Unique Function and Degradation of an Exotic Endogenous Opioid Peptide; DAT-Regulation of Nucleus Accumbens Microcircuitry by Oxycodone Exposure and Withdrawal
Species &Pain Class:(A,B) Mice
Question the Research Addresses: How do genetic insults (e.g., mutations associated with disease) and environmental factors (e.g., exposure to exogenous opioids) affect the function of striatal circuits, leading to abnormal behavior?

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

Comment: Please update the protocol to clarify the possible duration of food restriction for consistency. In the food restriction procedure, dietary restriction is described as lasting for a total of 14-140 days; however, in some experiments (such as experiment 2.1), restriction is described as occurring for 3-10 days prior to the start of up to 140 days of behavioral testing (for a possible duration of 150 days).

Comment: Please update the protocol to clarify the dose of fentanyl that will be administered to the mice in Experiment 1.1. In the experimental design layout, fentanyl treatment is described as occurring across three doses (0.1 mg/kg, 1 mg/kg, or 10 mg/kg), but in the attachment, fentanyl is shown as being administered at a dose of 0.1-1 mg/kg. Additionally, the "Drug Injection" procedure shows fentanyl as being administered only at a dose ranging from 0.1mg/kg to 1.0mg/kg.

Committee Decision: Stipulations must be met
For: 13 Against: 0 Abstain: 0

7. **Protocol Title:** 2110-39523A Development of a minimally invasive animal model of Legg-Calvé-Perthes Disease
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: Can we develop a targeted and minimally-invasive model of LCPD by injecting microspheres into the blood vessels supplying the hip in young domestic swine, and does this intervention induce vascular occlusion causing femoral head ischemia that will closely resemble LCPD.

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

   Comment: Please update the protocol to list what other embolic agents would be used other than microspheres.

   Comment: Please update the procedures to include the following: -Describe which peripheral vein will be used for placement of IV catheter. -Add that the animal will be intubated for procedures lasting over 15- 20 minutes to protect the animals airway and provide more precise delivery of the inhalant agent. This will also decrease environmental pollution for the staff. -Add type of heat source that will be provided to maintain animal's body temp while anesthetized. -Add how often vital signs will be recorded on the anesthetic record. -Add justification for following veterinary recommendations for anesthetic and analgesics regimes listed that are different from the preferred anesthetic protocol. When would an opioid CRI be used intra op? -Describe the use of SR buprenorphine in the post operative period. -Describe the repair of the carotid artery. -Describe why KCL is used for euthanasia under anesthesia as opposed to beuthanasia solution also listed.

   Committee Decision: Stipulations must be met
   For: 13 Against: 0 Abstain: 0

8. **Protocol Title:** 2110-39502A Studies in Heart Failure and Dystrophic Cardiomyopathy
Species &Pain Class:(A,B,C) Mice; (A,B,C) Mice
Question the Research Addresses: This research is focused on understanding the mechanisms that underlie the pathophysiology of dystrophic cardiomyopathy.

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 2)**

1. **Protocol Title:** 2003-37935A Novel ECMO Unit
Species &Pain Class:(B) Pig (Biomedical)
Question the Research Addresses: The objective of this study is to evaluate the swine as a model to demonstrate the functionality of TC-ECMO. The effectiveness of manual CPR on a fibrillating heart to maintain vascular pressure, blood gasses, and intracranial pressure will be compared to the effectiveness of using TC-ECMO.

   Committee Decision: Approved as submitted
   For: 13 Against: 0 Abstain: 0

2. **Protocol Title:** 2104-38973A Physiological-based Pharmacokinetics Approach to Determine the Extent of Drug Exposure of Antiseizure Medications During Pregnancy and Breastfeeding

   WITHDRAWN

Institutional Animal Care and Use Committee
Minutes
VCRC - 76D
12.14.21

Meeting Convened: 12:04 PM	Quorum Requirement: 10
Meeting Adjourned: 1:01 PM	Members Present to Vote: 18

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii	x	(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v9.0** 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 Items

1. The committee discussed a new protocol submitted by a lab whose previous protocol had been closed by committee vote. The new protocol does not appear to have taken veterinary and expert anesthesiologist advice into account and is not ready for review. Therefore, the committee voted to return the protocol with guidance to address the recommendations before resubmitting.

2. The committee discussed a request by an investigator to modify the lab's supervision plan. The committee approves the proposed change to anesthesia management but requests more information about the training of the proposed lab managers. The committee voted to approve the changes to lab supervision, pending IACUC leadership approval of the lab staff's training.

3. The committee discussed a self-report in which mice were ordered on the wrong protocol, resulting in surgery being conducted on a protocol for which it was not approved. The surgery and post-operative care were performed as outlined on the other protocol. Going forward, the lab has outlined a multi-step process for checking protocol numbers. The committee appreciates the detailed corrective action plan and considers the matter closed.

4. The committee discussed potential updates to the IACUC adoption policy, guidelines, and form. The current documents exclude use of the adopted animals for business, food or production, but there are cases in which such uses may be acceptable. It was also noted that there are additional items that should be updated in the policy. IACUC and RAR staff will update the documents and bring them back to the committee for approval.

5. The committee discussed the results of a recent member survey on preferences for continuing education. Based on the survey, meetings separate from full committee review will be scheduled for continuing education. Topics requested include conducting inspections and best practices for protocol review.

1. **IACUC-R1S1(# Protocols: 3)**

    1. **IACUC-R1S1 - NEW(# Protocols: 1)**

    1. **Protocol Title:** 2107-39283A Electroporation and Oncolytic Virotherapy for Pancreatic Cancer
    Species &Pain Class:(B,C) Mice; (B,C) Hamster
    Question the Research Addresses: How does electroporation and the timing of electroporation (relative to virus administration) affect adenovirus infectivity, replication and cell-killing effect of tumors in vivo.

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

    Comment: Please update the protocol to describe how sterility of instruments will be maintained between animals and how many animals will be undergoing surgery with one set of originally sterilized instruments. 2. Please include warm pad as part of recovery after anesthesia.

    Comment: Please update the protocol to describe how sterility of instruments will be maintained between animals and how many animals will be undergoing surgery with one set of originally sterilized instruments. 2. Please include warm pad as part of recovery after anesthesia.

    Comment: Please update the protocol to define more specifically and in more detail "moribund condition" as an experimental endpoint. Maybe some criteria can be combined together such as lethargy and unresponsive to a mild stimulus, indicate moribund condition.

    Comment: The justification for numbers of animals is insufficient. First, please update the protocol to include the

rationale for n=6. Second, the justification mentions a higher n will be used for those groups that have multiple time points - please itemize which conditions that applies to (it appears from the experimental design that the time courses are identical). There are 5 conditions noted in the justification - (control, virus monotherapy, electroporation monotherapy, virus + electroporation, electroporation + virus) - x 6 animals per group x triplicate = 90 animals. There are also several cancer cell lines mentioned. Please clarify how this will add up to 200 per strain.

Comment: Please clarify if the virus be expressing anything therapeutic? There is a comment in the protocol about 'control' virus, which raised the question. If they are delivering cargo, please include that information in the description of the experimental design.

Committee Decision: Stipulations must be met
For: 18 Against: 0 Abstain: 0

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 2)**

1. **Protocol Title:** 2106-39180A Immunopathology and adverse fetal outcomes after maternal viral infection T cells and cytomegalovirus-associated immunopathology
Species &Pain Class:(A,C) Guinea Pig
Question the Research Addresses: How do viral infections affect the placenta? How does the host immune response to either placental or fetal infection cause adverse pregnancy outcomes? How is the fetal immune system affected by prenatal exposure to viruses?

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

   Comment: Blood collection by toenail clip states 1 mL/collection; should this be µL?

   Committee Decision: Stipulations must be met
   For: 17 Against: 0 Abstain: 0
   Member 4 out

2. **Protocol Title:** 2007-38290A Safety and efficacy of Nov340 delivery of SaRNA in treating MPS I disease
Species &Pain Class:(A,C) Mice
Question the Research Addresses: We will address whether AAV-mediated gene therapy, or a combination therapy of stem cell transplant and oligonucleotide therapy can provide sufficient therapeutic enzyme to a murine model of MPS I.

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

   Comment: Please include information on the irradiator that is used, specifically the name of the machine.

   Comment: It is stated in the experiment design, Aim 1 that the mice will be given gentamycin administered via their drinking water to reduce potential infection from the bone marrow transplantation. Please add a corresponding "Dietary and Fluid Modification" procedure to this protocol for the gentamycin administration.

   Comment: The updated numbers in the species section to not appear to match the numbers in the experimental design tables. Please make sure these numbers are in alignment.

   Committee Decision: Stipulations must be met
   For: 18 Against: 0 Abstain: 0

Institutional Animal Care and Use Committee Minutes
December 28, 2021
VCRC - 76D

Meeting Convened: 12:00PM	Quorum Requirement: 10
Meeting Adjourned: 1:00PM	Members Present to Vote: 11

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

Non-Voting, Ex-Officio:

i		(O, U)
ii		(O, U)
iii		(O, U)

Institutional Veterinarian:

3	x	(M, V)

Correlates to Version **v9.0** 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 Items

No items were discussed

1. **IACUC-R1S1(# Protocols: 5)**

    1. **IACUC-R1S1 - NEW(# Protocols: 4)**

        1. **Protocol Title:** 2109-39463A Natural killer cells for the treatment of brain tumors
        Species &Pain Class:(B) Mice
        Question the Research Addresses: PI requests 660 class B mice for studies on immunotherapy for brain tumors. Glioblastoma (GBM) is the most malignant adult primary brain cancer and invariably lethal, without effective treatments. These animal studies would aim to assess the efficacy of Natural killer (NK) cells on GBM.

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

        Comment: Note that your volume here (3-8ul) doesn't match what is listed in the surgical procedure or the administration of cells procedure (3-5ul). Bupivicaine should not be dosed IP -- if the injectable form is used, it should go SQ.

        Comment: Note that the correct route for Bupivicaine is SQ or topical. It works as a local analgesic, so giving it IP would not help with incisional pain.

        Comment: Please change your routes for bupivicaine to SQ or topical.

        Comment: Please change your routes for bupivicaine to SQ or topical.

        Comment: Please change your routes for bupivicaine to SQ or topical.

        Comment: Note that if animals are too deep, the corrective action is to turn the iso down. Giving Yohimbine will not negate the effects of inhalant anesthetics.

        Comment: Please provide maximum volumes for gavage and IP injections.

        Comment: Given that the mice you work with are severely immunocompromised, what do you do to support them? Are they housed in full autoclaved housing? Are they handled differently? How do you navigate concerns around shared equipment, such as IVIS?

        Comment: Your methods of euthanasia look slightly different than what is descried in the Experimental Design section and procedure. Based on the protocol, you should have the following methods: - CO2 euthanasia, followed by cardiac stick or cervical dislocation - Anesthetic overdose (250 mg/kg Ket+ 12.5 - 25 mg/kg Xyl) followed by cardiac stick or cervical dislocation for secondary methods - "Other" euthanasia via perfusion under standard Ket + Xyl anesthesia (100 mg/kg Ket + 5-10 mg/kg Xyl)

        Comment: Within the experimental design section, it states that mice will be irradiated at a does of 0-20 Gy once a day for 2 to 14 days after implantation but within the irradiation procedure, it states irradiation will be given at a dose of 0-10 Gy once a day for 2 to 14 days. Please clarify the dosing range.

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

        2. **Protocol Title:** 2111-39566A Identification of American marten prey species using DNA barcoding
        Species &Pain Class:(B) American Marten
        Question the Research Addresses: PI requests 25 class B wild American Martens for a study to collect and summarize data on American marten diet and habitat selection to better understand diets of martens, including

the role of habitat use on diet, across the Western Great Lakes Region (WGLR). Specifically, we will describe broad-scale variation in American marten diets across the Western Great Lakes Region (WGLR) and evaluate factors influencing diet variation within and between study areas. We will use GPS location data to evaluate how habitat use influences prey selection throughout the WGLR, allowing us to identify which habitat types support marten prey species and foraging habitat.

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

Comment: Please specify what particular signs of injuries or abnormalities will monitored and how conclusion will be made whether they are capture related.

Comment: A couple of major points. First, I have serious concerns regarding the idea of collaring juvenile or yearling animals, unless there is a proven solution that mitigates strangulation risk from a loose collar. Unless there are good data supporting such a solution, I would object to collaring anything other than adult animals. Second, I have serious concerns regarding permanently collaring a free ranging animal. The Lotek Litetrack 20 RF GPS proposed for use here appears to be attached using zip ties, and I'm not sure how long these would last on the animal post study. Are there any data? Also, any data on mortality or other effects of permanent collaring on mesocarnivores of any type, let alone an active semi-arboreal animal like martens? For instance, are there relevant data from the previous radio collaring work done by the DNR? Is recapture of martens while the transmitter is still functioning not an option? I don't know if these animals become too trap wary after initial capture for this to be possible. Alternatively, is there no other collar material that could be used that would allow for collar failure soon (say within a year) after study completion? Some clarification of these points would be appreciated.

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

3. **Protocol Title:** 2111-39597A Pre-clinical models of low back pain
   Species &Pain Class:(C) Mice
   Question the Research Addresses: PI requests 1668 class C mice to for studies to i) understand how intervertebral disc degeneration leads to chronic low back pain and ii) explore mechanism-driven interventions for prevention and treatment.

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

   Comment: I don't feel that the method of euthanasia listed here matches what you have listed elsewhere in the protocol. Please add Decapitation under anesthesia (to reflect what you have described in your "Harvesting fresh tissue" procedure) and an "other" method which lists euthanasia via perfusion/exsanguination under anesthesia. In the fixation procedure you state that mice are deeply anesthetized prior to perfusion, but it does not sound like they are actually euthanized (lack of heartbeat).

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

4. **Protocol Title:** 2109-39442A Mechanisms to enhance the efficacy of cancer immunotherapy and the potential to reverse the resistance.
   Species &Pain Class:(A,B) Mice
   Question the Research Addresses: PI requests 2484 class A and 5004 class B mice for studies to address two basic questions, (1) Can prevention of immune exhaustion and enhancement of immune cell metabolism prevent the resistance to immune therapies? (2) How can standard of care therapies such as chemotherapies and immune checkpoint therapies be combined to prevent the induction of resistance to various immune therapies?

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

   Comment: Under question 2, it is stated that the lab staff will be monitoring the mice 2 to 3 times per week and that will increase to daily when the tumors reach 1 cm. However, later on it states mice will be monitored daily.

Please clarify that mice will be monitored daily by RAR or lab staff for distress in addition to monitoring their tumors.

Comment: Your answer to question 3 mentions cervical dislocation, but this method is not listed under question 2. Please reconcile.

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

2. **IACUC-R1S1 - AMENDMENT(# Protocols: 1)**

1. **Protocol Title:** 2003-37916A Inhibition of Opioid Tolerance
Species &Pain Class:(A,B,C) Mice; (C) Rat
Question the Research Addresses: PI requests to expand our assessment of the efficacy of non-opioid analgesics agmatine and agmatine-based therapeutics in a pre-clinical model of post-operative pain. We have requested approval to include these models in our program as well as several non-reflexive pre-clinical measures to assess analgesic effects including open field activity and conditioned place preference. Additionally, we have requested extended time points from 6 weeks to 8-12 weeks for studies of the effects of gene therapeutics on chronic pain in order to evaluate persistent analgesia expected from those therapeutics and to compare to our prior historic studies.

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

Comment: Please clarify if total number of animals need to be changed. Total number of animals produced in house not add up with new breeding procedure.

Comment: Please update research design in attachment to reflect: 1. New animals from breeding 2. Experimental procedures

Comment: Please provide viral load used in experiments in viral genome or genome copies. Additionally, experimental design suggests use of AAV but procedure indicate Adenovirus. Please correct for consistency.

Comment: Please provide range of viral load used in experiment in viral genome or genome copies. Additionally, experimental design suggests use of AAV but procedure indicate Adenovirus. Please correct for consistency.

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