**University at Buffalo**
**State University of New York**
**Office of Research Compliance**

**INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE**
**MINUTES OF THE MEETING**
**October 18, 2021**

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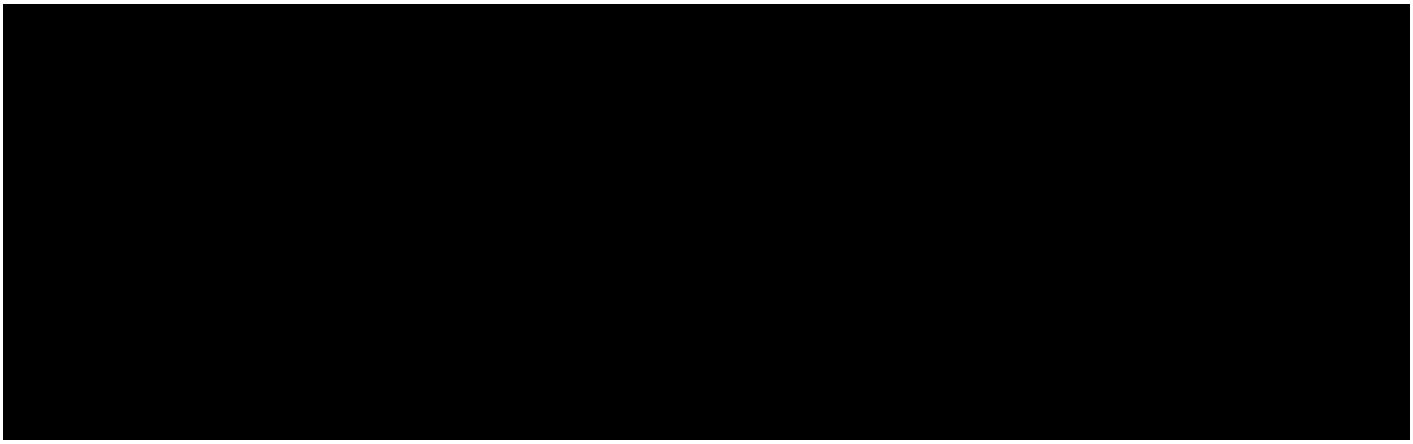
**ATTENDANCE:**



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**CALL TO ORDER:**

The IACUC Chair commenced the meeting at 12:32 PM.
If any member of the IACUC has submitted a protocol or amendment for review and approval, that member is not present during the discussion of and voting on their protocol or amendment. Quorum is maintained.

**PRESENTATION OF THE MINUTES:**
The minutes of the 2021 IACUC September meeting were presented. The September meeting minutes were voted on and unanimously approved.

**BUSINESS:**

Possible non-compliance PROTO201900198: Per Attending Vet: It was brought to my attention that the six pigs in rooms B2103 and B2104 have all been infected with MRSA. The LAF care staff, veterinary staff or IACUC members (who inspected these rooms this week on the semi-annual review) knew that these animals had been infected with MRSA. Three of these pigs have been infected for over a week and the LAF staff at JSMBS had no idea. There is a MRSA biohazard sheet in each of the pig binders that needs to be hung on the door when the room becomes infected. The chance of infection to humans is small, but we have procedures in place that must be followed to comply with University policies for Biohazardous agents.
The issue was sent to EHS and the committee decided that was not an IACUC non-compliance issue.

PTE53041N: OLAW requested a meeting regarding timeline clarifications to the Noncompliance PTE53041N.

Semi-Annual Inspection October 2021:
Fall 2021 Program Review: Currently, the IACUC request that monitoring charts are submitted at the completion of each experiment and are either submitted to the LAF or the IACUC administrative office. Dr. Martin reviews all the monitoring charts and sends the IACUC administrative office a statement regarding the monitoring charts. The statements are then in turn entered into a spreadsheet titled "Protocols with Category E monitoring charts" in UB Box under IACUC Documents and Spreadsheets. All committee members have access to the "protocols with Category E monitoring charts" spreadsheet. In addition, the committee request a sample of a category E monitoring chart during the annual. Some PIs have commented that this process is redundant.
The committee reviewed the monitoring chart procedure. Going forward any category E annuals will be assigned to committee members for review. Twice a year a general email will be sent out, reminding PIs to submit their monitoring charts. Also twice a year category D monitoring charts will be reviewed. The committee will still ask for a sample of monitoring charts during the category E annuals.

The Fall 2021 Semi-Annual Inspections and Report to the IO:
Most of the deficiencies have been resolved and no significant deficiencies were found. A draft of the Fall 2021 Semi-Annual Report to the IO was included for review. The committee reviewed the document and it will be distributed to be signed digitally. Once all the deficiencies have been resolved the report will be sent to the IO.

AMEND202100262: The committee felt that the amendment cannot be approved because a stronger scientific justification is needed for reducing the acclimation period. Some references were provided, but many were not relevant to the species being used in the studies (mice). The PI needs to provide additional justification for the requested change.

AMEND202100264: The committee felt that the amendment cannot be approved because a more robust scientific justification is needed for reducing the acclimation period. Some references were provided, but many were not relevant to the species being used in the studies (mice). The PI needs to provide additional justification for the requested change.

AMEND202000010: The committee concluded that the experiments proposed in the amendment are too significant to be considered as an amendment. Rather, a new protocol (s) should be created to be reviewed as a standalone study.

DOH Inspection: The DOH inspected lab space at BEB, BRB, RIA and Park Hall. At BEB, they found that laboratory staff were not using appropriate PPE. One student was conducting a surgery while watching a zoom meeting or online class. At RIA, one PI was storing controlled drugs incorrectly and they didn't feel that surgical areas were sufficient for sterile surgery. At Park, the inspectors observed 3 different people using the same anesthesia machine and one staff member using their phone while conducting a surgery. A final report will be forthcoming from the DOH.

It was reported to the IACUC that laboratory staff at Park felt intimidated and distracted by the DOH Inspectors. They were asking questions in an imposing manner while staff were conducting their complicated surgeries. One staff member reported that they ripped a jugular vein while trying to insert a catheter due to the questioning. One PI said that he and his staff welcome observers during surgeries, but to reduce stress and distractions it would be good if the inspectors either held their questions and comments until the end of the surgery or consult the protocol for specific procedural details. Being

cognizant of the surgeons' personal space would increase the success rate of the surgeries (and subsequent animal welfare) as well. Finally, the inspectors seemed to be under the impression that animals were being induced at 1% isoflurane, which is not the case. All animals are induced at 3-5% isoflurane using the EZ-190F Auto-Flow Anesthesia Machine. This system is designed for providing anesthesia for multiple animals; note that in over 800 surgeries there have been no deaths attributed to anesthetic overdose (the lab's mortality rate is 0.6% and improving; deaths only occur following surgical complications, not anesthesia problems) or animals being revived during surgical procedures (all animals are pinch-unresponsive during the entire surgery).

**APPROVALS:**
A list of the submissions approved since the last meeting has been presented to the committee.

**ANNUAL RENEWAL SUBMISSIONS:**

**No Category E annual submissions**

**PROTOCOL REVIEW:**

In addition to the IACUC review, Environment, Health & Safety (EHS) has also reviewed all protocols and amendments submitted this month. For protocols involving the use of hazardous agents in live animals, their use will be approved by the appropriate EHS authority and, as appropriate, laboratory SOPs will be placed as recommended by EHS prior to IACUC approval.

1. **PROTO202000010**

**Protocol Summary:** From PI's non-scientific summary: Implantation of Tissue Engineered Vessels (TEVs) in a large animal growth model. Acellular TEVs have been engineered in my laboratory and these studies aim at testing their implantability into a physiologically relevant animal model, namely ovine. The experiment "Implantation of TEVs" needs edits and clarifications to Buprenorphine administration and ketamine dosage. The donor cuff surgery needs clarifications to the survival of the donors, amount removed, dosage of anesthesia and analgesia.
**Committee Discussion:** Edits and clarification need to be made in Click. The PI needs to try and obtain appointments for the individuals who are listed under external team members. The x-ray facility being used needs to be clarified. For the "Anesthesia-Ketamine/Xylazine- Sheep" procedure buprenorphine should be re-administered every 4-6 hours, rather than every 8 hours in sheep and the ketamine dose needs clarifications. Clarifications need to be made to the "Donor Cuff Surgery" regarding survival, removal, to ketamine and buprenorphine dosage.
**Committee Action:** The committee unanimously voted to require modifications to secure approval and to allow the revised protocol to be reviewed and approved by Designated Member Review.

2. **PROTO202100042**

**Protocol Summary:** From PI's non-scientific summary: This study is designed to test the requirements for development of periodontal disease, including the interactions between both general bacteria and specific bacterial and various components of the immune system through the use of a ligature (thread) tied around teeth and oral gavage model.
**Committee Discussion:** Edits and clarification need to be made in Click. The experiment "Mouse breeding" needs clarification to the strains that will be bred, a stronger justification, pain category and a euthanasia procedure needs to be added. The experiment "Mouse infection" needs a list of strains, more information regarding how groups will be delineated, oral gavage, clarifications need to be made

to anesthesia and additional procedures need to be added. The procedure "P. gingivalis, S. gordonii and T. denticola administration" needs clarifications to the experimental timeline and gavage procedure needs more information. The procedure "Euthanasia" needs clarifications to the euthanasia rate and a secondary method of euthanasia. The procedure "Antibiotic water" needs clarifications to the frequency of the water bottle change and Kanamycin needs to be listed by name. Personnel need to add their animal research experience. The alternative section needs more research. The housing section needs clarifications.

**Committee Action:** The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

### 3. PROTO202100071

**Protocol Summary:** Taken from the PI's non-scientific summary: Sjogren's syndrome is an autoimmune disease in which salivary gland function is lost because of attack by the immune system. We have demonstrated that the spleen is critical for development of Sjogren's syndrome in IL14a transgenic mice (TG), which suggests that cells causing damage to the salivary glands are educated in the spleen. We will evaluate which cells must traffic between the spleen and the salivary glands for Sjogren's syndrome to occur.

**Committee Discussion:** Edits and clarification need to be made in Click. The breeding experiment needs clarifications to animal numbers, how mice will be bred, supportive care needs to be added, procedures need to be added and the pain category needs to be clarified. The specific aim 1 and aim 2 needs clarification to animal numbers, procedures moved to a different experiment and to the procedural timeline. All antibodies listed in procedures need to be described in a substance administration. The procedure "Drugs for Saliva Collection" needs clarifications to IP injection, needle size, animal positioning during saliva collection and if fasting is necessary. The procedure "Saliva Collection" needs clarifications to animal positioning during saliva collection and if fasting is necessary. The procedure "Euthanasia via CO2" needs clarifications to time of euthanasia. The breeding and housing sections need clarifications.

**Committee Action:** The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

### 4. TR202100043

**Protocol Summary:** Taken from the PI's non-scientific summary: 1) The goal of our research is to investigate the underlying connections between the reward and circadian systems. Diurnal variation in reinforcement-related process related to addiciton has been described in models of place preference, self-administration, and sensitization. This variation hints at modulation by a hormone and/or molecule under circadian control. We will utilize a two-step approach, first examining the role of melatonin (endogenous and exogenous) and its receptors in the modulation of reinforcement-related behaviors and secondly examining the contributions of the reinforcing stimuli of palatable food (Snack), drugs (psychostimulants), and running wheel to induce rhythmicity. Studies have suggested a circadian variation in natural reinforcement. The pineal hormone melatonin is synthesized following a circadian rhythm, with low levels during the day and high levels at night. 2) The reinforcing properties snack food and reinforcing drugs (psychostimulants) will be measured by the conditioned place preference paradigm, which relies on the association of a reinforcing substance with a distinct set of contextual cues. These studies will take place during the day (Zeitgeber Time [ZT] 6 – 8; 12h: 12h light-dark cycle, ZT 0 = lights on), when melatonin is low and during the dark phase (ZT 19 – 21), when melatonin is high. 3) Reinforcement-related behaviors are highly dependent on learning and memory processes. Therefore we will also assess the contributions of melatonin (endogenous and exogenous) and its receptors on learning and memory. We will accomplish this thourgh use of the novel object

recognition task and the attentional set shift task. 4) Palatable food as well as methamphetamine access has been shown to alter circadian rhythms through an extra-suprachiasmatic nucleus (SCN) oscillator termed the Food Entrainable Oscillator (FEO) or Methamphetamine Sensitive Circadian Oscillator (MASCO) respectively. Running wheel activity, which is also known to have reinforcing properties, is frequently used to measure the output of the circadian system. We will examine the role of running wheel in the induction and maintenance of rhythmic behavior in SCN lesioned mice (SCNX). We will also attempt to locate the brain region housing this oscillator through use of dorsomedial hypothalamus lesioned (DMHX) and habenula lesioned (HbX) mice. All together this work will elucidate and provide mechanistic understanding for the role of melatonin in regulating reward processes, the variation of reward learning across a 24 hour period, the relationships between reward learning and the circadian system, as well as potential brain areas controlling these processes.
**Committee Discussion:** Minor edits and clarification need to be made in Click. For each experiment a simple calculation for to account for the number of mice needs to be added. The procedure "Condition Place Preference (CPP)" needs clarifications to the apparatus used for CCP and what occurs during the test. The procedure "Avertin" needs clarifications to when Avertin is given. The procedure "Pentobarbital Euthanasia (Overdose)" and "Buprenorphine" needs edits to dosage. The procedure "Attentional Set Shift (ATSS)" needs a behavioral test description. The surgery "Electrolytic Lesions of Suprachiasmatic Nucleus (SCNx)" needs edits to the use of Pentobarbital for anesthesia and buprenorphine dosage, the committee recommends the use of sutures to close the skin incision and not apply ointments to surgical wounds. The experiment "G) Modulation of DOI Induced Head Twitch Response (HTR) by the Melatonin System" needs substance administrations added and clarifications need to be made to experiments that analyses for head twitching and locomotion. The Alternatives and Duplication section need to be updated. A scientific merit form needs to be added and all the old amendments from 2015-2017 need to be removed.
**Committee Action:** The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

**5. TR202100044**

**Protocol Summary:** Taken from the PI's non-scientific summary: There is a strong need to understand regional distribution of antibody in brain and quantitatively characterize the relationship between systemic antibody concentrations and concentrations in different part of the brain using a physiological pharmacokinetic (PK) model. Towards this goal, brain microdialysis studies will be performed in rat, to determine the concentrations of endogenous antibody in different compartments of the brain (i.e. striatum for sampling brain extracellular fluid (ECF), lateral ventricle, and cisterna magna). Additionally, drugs (e.g. AAVs expressing different proteins, trastuzumab and OX26) will be injected in the rats, and its PK will be determined in brain ECF, lateral ventricle, and cisterna magna, using microdialysis.
**Committee Discussion:** Minor edits and clarification need to be made in Click. Clarifications need to be made to the strain of animals that will be used. The procedure "Anti-NMDAR1 antibody administration" needs clarifications to the anesthesia for the IV injections. The procedure "Anti-NMDAR1 antibody administration", "Brain Microdialysis (Anti-NMDAR1), Brain Microdialysis of AAV mediated antibody expression and "Brain Microdialysis (OX-26)" needs clarifications to the procedural timeline. The surgery "Jugular vein and Femoral vein cannulation" needs Bupivacaine added, clarifications to suture method and finishing line usage and induction levels need clarifications. The procedure "Drug Dosing" the use of pharmaceutical grade drugs needs to be clarified. The procedure ": Drugs for Jugular & Femoral Vein Cannulation" needs clarifications to drug and saline

volume. If the animals will undergo multiple surgeries needs to be clarified. The animal justification needs more information. The housing section needs clarifications.
**Committee Action:** The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

The IACUC Chair adjourned the meeting at 2:52 PM.