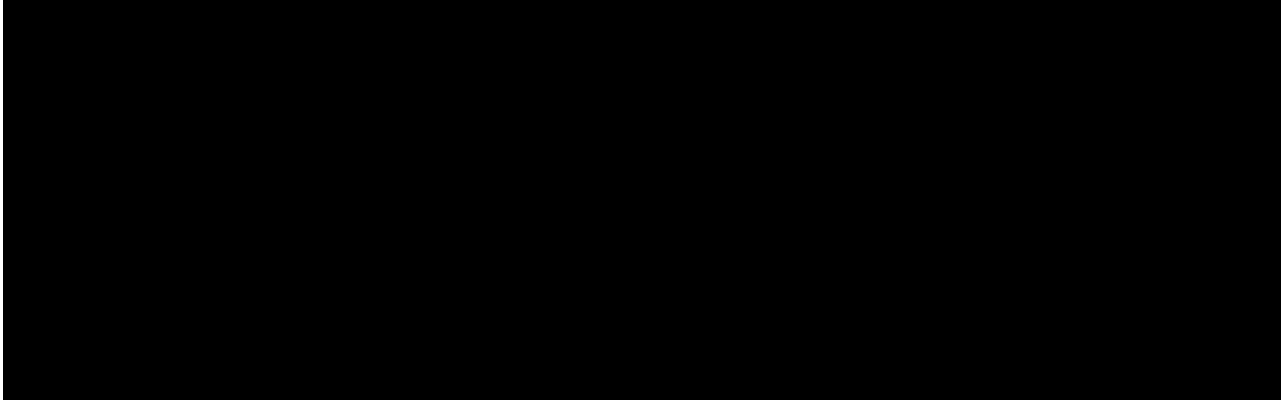


**University at Buffalo
State University of New York
Office of Research Compliance**

**INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
MINUTES OF THE MEETING
June 21, 2022**

ATTENDANCE:



CALL TO ORDER:

The IACUC Chair commenced the meeting at 12:33 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 2022 IACUC May meeting were presented. The May meeting minutes were voted on and unanimously approved with the correction of two typos.

ANNUALS

A list of annual renewal submissions are provided in the CLICK system.

For protocols involving Pain Category E procedures, the PIs have been contacted and asked to provide the number of animals used over the past year for these procedures, summarize the monitoring regimen for these animals, indicate whether or not a monitoring chart/record is used, provide a copy of this record, indicate if there were any unexpected occurrences (i.e., problems, deaths), and confirm that these occurrences were reported to the LAF veterinary staff.

BUSINESS:

Category E annual submissions: Submissions are listed under protocol review.

AAALAC Site Visit Summary: The University is working on the AAALAC site visitors' recommendations to improve the animal use program. The AAALAC must see the harm/ benefit highlighted in the meeting minutes, alternatives suggested to PIs that have departures from the guide, and reevaluate water restrictions. Many of the water restrictions that were documented in Click are water scheduling.

Category E policy: The committee discussed the possibility of creating a category E policy to clarify PIs on what procedures are considered category E and the IACUC expectations category E procedures. It was suggested that a policy be drafted and sent to the PIs with category E procedures to allow PIs to ask questions and provide feedback.

New Policy Proposal "Policy on the use of Animal Tissues or Carcasses": The committee noted that minor edits were needed for the new policy. The corrections will be made and emailed to the committee for approval.

Policy Review "Policy on IACUC Training Requirements for Research Personnel": The attending veterinarian submitted modifications to the current training policy to address vivarium card access and BSL 3. The committee noted that minor modifications are needed. The corrections will be made and emailed to the committee for approval.

Noncompliance PMY41040Y: The PI submitted a response stating that the tail snipping procedure of mice greater than 21 days was in the protocol. The PI is disputing that portion of the non-compliance but agreed that the lack of topical and systemic analgesics is a significant animal welfare issue immediately addressed with the lab. The PI submitted an amendment clarifying the procedure in Click and had the lab staff sign an attestation form stating that they read and understood Laboratory Animal Facilities (LAF) SOP 2.A.9. The committee determined that the procedure was listed in the protocol, but not providing the animals with topical or analgesia was a non-compliance. The committee reviewed the corrective actions taken by the PI and determined no further action is needed. Letters will be sent to government agencies and accrediting bodies stating that the IACUC is satisfied with the PI's corrective action.

PROTO201800154 Noncompliance/ Colony Management: The PI submitted the attestation form stating that they read and understood LAF SOP 2.A.9. and the requested breeding colony management paperwork. The committee reviewed the documents and determined that the PI is moving forward in the correct direction regarding breeding colony management. The committee requested that the PI still submit breeding colony management paperwork for the time being. Letters will be sent to government agencies and accrediting bodies stating that the IACUC is satisfied with the PI's corrective action.

Facilities Noncompliance/ Animal Welfare Concern: The committee reviewed the Director of Facilities Operations' corrective action to prevent the humidity issue from reoccurring in the animal holding rooms. The committee accepted the plan and determined that no further corrective action is needed. A letter will be sent to OLAW closing the noncompliance.

PAM Site Visit: The new PAM Officer conducted a training site visit with the previous PAM Office and submitted the documentation for review. The report was well done, and the committee did not have any suggestions for improvement.

Continued Education Training: The PAM Officer took the CITI PAM course and present what they learned in a PowerPoint presentation to the committee.

AMEND202200191 amendment for ENS03077N and AMEND202200192 amendment for ENS04097Y: The same PI submitted both amendments. The DMR reviewer called FCR due to the recent AAALAC site visit requesting refinement for departures from the guide. The study animals are housed in wire bottom cages to monitor food intake. The PI was asked to place resting boards in their wire bottom cages. The PI was concerned anything edible would interfere with the study or the excrement would mix with the food. The committee determined that the PI's concerns were viable and would ask the PI to conduct a pilot study to determine if a resting board would interfere with the study. The committee will review the results of the pilot study in approximately six months.

AMEND202200146 amendment for PROTO202100025: The lab is requested to use a euthanasia method not approved in the AVMA guidelines for larger cold-water fish. The committee determined that they would not approve the amendment, and the lab will need to use a euthanasia method that is AVMA approved.

Departures from the Guide: The committee reviewed "The Guide" regarding specific departures, including single housing, wire-mesh flooring, and water restrictions.

APPROVALS:

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

PROTOCOL REVIEW:

In addition to 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. AR2022000052 (Annual Review for RIA13095Y)

Annual Summary: Since the beginning of May 2021, 297 rats and 210 mice have been generated or purchased from vendors (for non-category E usage). The majority of the mice have been used for breeding purposes to maintain our colony of transgenic fatty acid-binding protein knockout mice as well as the following approved experiment:

- Effect of Fatty Acid Binding Protein (FABP) 5 and 7 knockout on behavior and reward

The majority of the rats were used for the following approved experiments:

- Effects of Prenatal THC and/or Nicotine exposure on metabolic disease/obesity, attention/memory and related behaviors in offspring

- Neurochemical and behavioral effects of chronic methylphenidate

Treatment Since the last annual renewal, the only unanticipated health concern was dermatitis behind the right ear in one mouse and developed corneal ulcer in another mouse. This was communicated in email with a UB Clinical Vet on March 1 2022.

In May of 2021, 19 mice were subjected to an unpredictable chronic mild stress (UCMS) procedure that falls under category E for a period of 4 weeks. This procedure was part of our previously approved experiment, "The role of FABP7 on chronic unpredictable mild stress". Following the completion of the study, this experiment was subsequently removed from our RIA13095Y protocol.

The following observational monitoring procedures were performed during the 4 week UCMS procedure:

- Daily examination of spontaneous movement in home cage
- Daily monitoring for any abnormal appearance or behavioral effects (e.g. coat appearance, trembling)
- Daily monitoring during and following all mild stress procedures
- Body weight measurements taken every 3 days
- Body condition scores taken every 3 days

Attached as a comment includes our spreadsheet created last year to document stressors used, dates of stressors, body weights, body condition scores, notes on movement, physical appearance, and condition following each stressor.

Mice undergoing the UCMS procedure did not show diminished body weight nor did any mice meet exclusion criteria based on the above monitoring procedures that would merit removal from the study.

Committee Discussion: The committee reviewed and discussed the harm versus benefit of the category E procedures. The Committee reviewed the procedures and assigned a couple of additional procedures as category E. The committee requested that the PI appropriately redistribute the animal numbers. Additionally, references to procedures that are no longer listed need to be removed. The committee requested the PI update the alternatives search section of the protocol.

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. TR202200017 (NSG01033N)

Protocol Summary: From PI's non-scientific summary: The objective of this renewal submission is to compare the effects of potentially neuroprotectant treatments, following temporary and permanent occlusion of the middle cerebral artery, the most common location for stroke to occur in humans. Rats will be used as the model because they are the most applicable to human disease.

Committee Discussion: Edits and clarifications need to be made in Click. Substance administrations need to be added to the protocol. Departures from the guide were discussed, and clarifications were requested. Experimental timelines need to be added or need clarifications. The triennial review summary was missing important information, and the committee asked for additional information. The committee questioned the need for a "Sham Experiment" the PI is requested to reconsider the experiments or provide additional information on why the experiment is necessary. The PI was asked to review the justifications for single housing to ensure they are all necessary. The committee noted that multiple experiments have similar descriptions. The PI was requested to provide a unique description for each experiment. The behavioral procedure "Rat Stroke Neuro Scores" needs more details. More details need to be added regarding the use of cold sterilant. There are references to glioma cell research in several places, which seem to be misplaced, and the committee requested clarifications. Several experiments need clarifications and edits. The animal justification section needs to be updated. Alternatives need to be researched for each category D procedure. A current search needs to be made for the duplication section. The housing section needs to be updated, and an updated scientific merit form needs to be uploaded to the protocol.

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.

3. TR202200018 (PMY49120N)

Protocol Summary: From PI's non-scientific summary: We have two lines of research, both of which focuses on identifying and testing potential drug candidates for future development of clinically-used medicine. The first line of research (Aim 1) will focus on testing the pain-relieving effects of a new class of compounds that specifically target on $\alpha 2/3$ -GABA_A receptors. Chronic pain is a huge clinical issue and existing analgesics are insufficient for clinical needs. Recent opioid epidemic makes the development of non-opioid non-addictive analgesics a more pressing task. Working with a chemist, we have identified compounds that specifically act on $\alpha 2/3$ -GABA_A receptors, a receptor that is important to control pain signal from the peripheral tissue to the brain, which demonstrated selective analgesic activity without typical side effects. In the future three years, we will systematically test the efficacy and safety of these compounds against chronic pain and examine whether they will be good candidates as adjuvant drugs along with clinically used analgesics (i.e., Tylenol, Lyrica and opioids) as combination therapies. Successful execution of these compounds will provide valuable information for further development of these compounds and new compounds with similar pharmacological profiles as novel pain analgesics. The second line of research (Aim 2) will test the potential anti-addiction effects of TAAR1 agonists. Addictive substances such as cocaine, nicotine and methamphetamine are highly deleterious to human health and there are few effective treatments available. Our earlier research has identified TAAR1 agonists are potentially highly effective treatment to treat drug addiction. Studies in the future three years will continue to examine the therapeutic potential of TAAR1 agonists against cocaine and nicotine addiction. We will also examine the anti-addiction effect of corydalmine, a naturally-occurring compound that can be found in many plants, against methamphetamine. Successful execution of these studies are expected to validate TAAR1 agonists and corydalmine as lead compounds for further development of drugs for the treatment of drug addiction.

Committee Discussion: The committee discussed harm vs. benefit for the category E procedures. The committee reviewed and discussed departures from the guide. Edits and clarifications need to be made in Click, and questions left blank must be completed. Substances and substance administration need to be added to the protocol. The multiple survival surgeries tab was clicked, but no additional information was added to the protocol. The committee requested clarifications regarding the multiple survival surgeries. The euthanasia procedure needs to be updated with the new AVNA euthanasia guidelines. The committee has requested a scientific justification for the use of CO₂ over other methods of euthanasia. The experiment "1A" needs clarification on the number of animals undergoing the category E procedure. The committee requests a five-day minimum habituation period for experiment "1B" survival procedures."

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.

4. TR202200019 (MIC14103Y)

Protocol Summary: From PI's non-scientific summary: The objective of this renewal submission is to further our understanding of how regulatory T cells (Tregs) are lost during *T. gondii* infection. Tregs are a crucial part of the body's immune response to parasitic infection and their loss in *T. gondii* infection is part of the emergence of tissue damage in the bowel. We also aim to determine what factors are important for bringing back Tregs after recovery from infection. Mice are used because they are a natural host for the parasite and easy to work with.

Committee Discussion: The committee discussed harm vs. benefit for the category E procedures. The committee reviewed and discussed departures from the guide. Edits and

clarifications need to be made in Click. The committee recommended removing references to Veterinarians no longer employed at the University. The committee requested that the SDS sheets for EdU and Tamoxifen be added to the protocol. The committee suggested the PI could increase the weight loss of irradiated mice by 5% of carefully monitored. The committee recommended changing all breeding mice with an ear tagging to category C and breeding only mice without an ear tag to category B. Alternatives need to be searched for all category D procedures.

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.

5. TR202200020 (PROTO201900069)

Protocol Summary: From PI's non-scientific summary: Ischemic heart disease continues to be the leading cause of mortality and morbidity in the United States, impacting the lives of millions of people each year. This project seeks to identify novel therapeutic approaches and targets to simulate heart muscle regeneration, including those that would not require the administration of stem cell populations. This would enhance the treatment of patients with a wide spectrum of cardiac disease including heart failure and myocardial infarction.

Committee Discussion: Edits and clarifications need to be made in Click. The committee reviewed and discussed departures from the guide. The committee requested the approximate number of animals used to be added to the triennial review summary. The committee asked for clarifications regarding the use of proparacaine in the procedure "Blood Draw."

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.

6. TR202200021 (ENS01086Y)

Protocol Summary: From PI's non-scientific summary: The objective of this proposal is to uncover the mechanisms by which the ventral tegmental area amylin receptor activation reduces food intake. We will identify the signaling molecules that communicate with amylin in the brain and what induces these signals and through behavioral studies, will establish the ability of this signaling to modulate food intake. We will also investigate other mechanisms of neural and hormonal controls of food intake in rodents under this protocol.

Committee Discussion: The committee reviewed and discussed departures from the guide. Edits and clarifications need to be made in Click. The committee recommended removing any post-mortem procedures. Substances and substance administrations need to be added. NPG forms need to be added to the protocol. References to the "old paper" paper protocol need to be removed. Procedural timelines need to be updated. The husbandry exceptions for water and food restrictions were reviewed. It was noted that the restrictions were a short and long-term fasting period. The committee recommended moving it from water restrictions under husbandry exceptions. The committee recommends small resting boards for experiments that spend the experiment in wire bottom cages. The committee requested more details regarding prolonged restraint. All rats undergoing a prolonged restraint procedure need to be listed as category E. Rats not undergoing prolonged restraint in the experiment "Acute stress and food intake" can be category C. Monitoring parameters need to be added to the procedure "Scheduled limited water access." The committee has requested a scientific justification for the use of CO2 over other methods of euthanasia. The alternatives section needs to be completed for all category D procedures, and transcranial perfusion can be removed from the alternatives section as it is a category C. The committee requested that if an alternative to procedures would result in less

pain and/or distress, the PI will need to provide a reason why they cannot be used or are inappropriate for the study.

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.

7. TR202200022 (PROTO201900078)

Protocol Summary: From PI's non-scientific summary: The research uses mouse models to understand the gene regulatory mechanisms that govern generation of diverse neural cell-types with specialized function and connection pattern during central nervous system development and to understand how disruption of these processes leads to various neurodevelopmental disorders in humans.

Committee Discussion: The committee discussed harm vs. benefit for the category E procedures. The committee reviewed and discussed departures from the guide. Edits and clarifications need to be made in Click. The SDS sheet for tamoxifen needs to be added to the protocol. The triennial review summary needs additional information and clarifications. Substances and substance administrations need to be added to the protocol. The committee recommends that Septocaine be applied before drilling holes. The committee recommends adding ropivacaine as an alternative to bupivacaine since bupivacaine has been back-ordered for most of 2022. The committee has requested a scientific justification for the use of CO2 over other methods of euthanasia. A more substantial justification needs to be added to the toe clipping procedure. "Live Tissue Collection (mouse)" should be renamed "Ear Punch/Ear Tag." The procedure "Recombinant plasmid mixture (rabbit)" needs information on the use of CFAs, more robust scientific justification for CFAs needs to be added, and monitoring parameters need to be outlined. The committee recommended alternate euthanasia methods for the rabbits. The antibody procedure needs edits and clarifications. Any controlled drugs must be in the "controlled drug" tab selected in Click. The Fatal Plus administration needs additional information. The committee recommended the PI allow for the option for either epaxial or hind limb muscles for IM injection. Husbandry exceptions and enrichment need to be clarified. The age and gender of the animals being used need to be clarified in a couple of the experiments.

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.

The IACUC Chair adjourned the meeting at 3:51 PM.