

2/14/2020

## NIAAA ACUC MEETING MINUTES

January 29, 2020

The NIAAA Animal Care and Use Committee (ACUC) convened on Wednesday, January 29, 2020 at 1:30 p.m., [Redacted by agreement]

### Attendance

#### Members:

<input checked="" type="checkbox"/>	Dr. Bin Gao	Chairperson, LLD
<input type="checkbox"/>	[Redacted by agreement]	
<input checked="" type="checkbox"/>	Dr. Raouf Kechrid	Attending Veterinarian, OLAS
<input checked="" type="checkbox"/>	[Redacted by agreement]	
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☒ Present ☐ Absent

#### Guests:

[Redacted by agreement] (OACU Observer)

### 1) Old Business

- The committee reviewed and approved the December 17, 2019 ACUC meeting minutes as written.
- **Physical plant**
  - Replacement of door sweeps: The replacement of door sweeps within the [Redacted by agreement] [Redacted by agreement] began on January 21<sup>st</sup>, 2020 and was completed today (January 29<sup>th</sup>, 2020) at noon. Topic closed.
  - [Redacted] Renovations: Renovations to room [Redacted] started in the [Redacted by] on January 27<sup>th</sup>, 2020 and were completed today (January 29<sup>th</sup>, 2020). The storage room has been successfully converted into a procedure room and the process of moving equipment for 3 laboratories from [Redacted] into this new shared procedure space may now begin.

## 2) New Business

- **Introduction of** [Redacted by agreement] was introduced to the Committee members as the new ACUC Observer from the Office of Animal Care and Use (OACU) that will be attending our NIAAA ACUC meetings in the future.
- **SOP 4250 – Training Animals:** This SOP was last reviewed and approved by the ACUC on February 2017, therefore, it was included in the current ACUC agenda for its triennial review. The Facility Veterinarian gave a brief overview of the SOP and the goals and procedures, which have not changed since the last review. A Committee member asked a question about the meaning of culled animals and the Facility Veterinarian explained the use of this term. No changes to the SOP were suggested and the ACUC approved it as written.
- **Animal Irradiation Handbook:** An Animal Irradiation Handbook was created by the NIAAA OLAS to outline irradiation procedures for investigators that have irradiation of animals approved on their ASPs. This information was previously provided in an SOP format. The FLAC SOPs are intended to be used by the facility staff, but most of the information included in this SOP was intended for the investigators and was not applicable to the FLAC staff. The OLAS decided it would be better to alter the format and create the Handbook, which is more relevant for the intended audience. The information did not change from the SOP to the Animal Irradiation Handbook; however, it was simplified and reorganized. The ACUC reviewed the new Handbook and agreed with its content. The Animal Irradiation Handbook is posted on the OLAS SharePoint site for access by all investigators.
- **Minor Updates to Investigator Orientation Handbook:** The Investigator Orientation Handbook was revised to clarify the cage sanitation procedures and our NIAAA ACUC approved performance standard described on page 16 of the Handbook. A facility-wide extended change frequency for filter tops and wire-bar lids used on micro-isolation style caging was previously implemented. This approved performance standard allowed cleaning and changing of these items monthly. This also includes stainless steel feeders that may or may not be integral with the wire bar lids, so these items were specifically mentioned in the Handbook as well to clarify the current procedures.
- **AAALAC PD to include appendices due 2/15/2020:** The Committee was reminded that the Office of Laboratory Animal Science (OLAS) continues to review and update the NIAAA AAALAC PD in anticipation of the upcoming June 2020 AAALAC site visit. The OACU provided comments regarding the first submission of our AAALAC PD and the second submission is due back to the OACU on February 15<sup>th</sup>, 2020. This submission will also include all of the completed appendices.
- **Resignation of the** [Redacted by agreement] **Facility Manager:** The Committee was informed that the [Redacted by agreement] Facility Manager resigned and his last day will be on February 7<sup>th</sup>, 2020. The Contractor is actively searching for a replacement, but the Assistant Facility Manager will be filling this role in the interim.

- Animal Use Database – Stopping Cards:** The Committee discussed the Animal Use Database and the necessity of scanning animal cards to stop them in the database once the animals are no longer present in the [Redacted by agreement]. Currently, animal cards are scanned out and inactivated in the database as they are turned into the [Redacted by agreement] front office by investigators. The data from the Animal Use Database is then posted to the OLAS SharePoint site at least once per week for investigators to reference. The Committee was asked if they find this data useful and whether they need the date a card is inactivated to be recorded. The database is not currently accurate with respect to the number of animals that are presently in the [Redacted by agreement] as there are many more active cards in the database than there are animals in the [Redacted by agreement]. A comparison between the manual animal census taken by the [Redacted by agreement] staff monthly and the list of active cards in the Animal Use Database shows this discrepancy. Examples from the currently posted active card data and the January 2020 manual animal census were shown to the Committee as a representation of this discrepancy. The OLAS has identified that this issue is primarily caused by investigators choosing to keep their animal cards rather than turn them in to be inactivated in the database. Members of the Committee commented that many of the investigators write important information on these cards and this is likely why they choose to keep them. The OLAS does not require investigators to turn in the animal cards once they are removed from the [Redacted by agreement] and OLAS does not retain the cards once they are inactivated, so it is extremely difficult to keep the active card data accurate. The investigators also do not have the opportunity to scan the cards out of the database themselves due to the limitations of our network accessibility. This may be an issue that can be corrected in the future, but if the date of card inactivation is not useful to the investigators, OLAS proposed discontinuing the process altogether. The ACUC members commented that they do not need this information and do not oppose discontinuing the process. Moving forward, animal cards and breeder cards will no longer be regularly inactivated in the Animal Use Database. However, every six months groups of animal cards that are greater than 24 months old and not currently housed in the [Redacted by agreement] will be stopped in the database.

### 3) Animal Study Proposals

- The following ASP was reviewed by Full Committee Review (FCR) at a convened meeting of a quorum:

- i. [Redacted by agreement]
 

[Redacted by agreement] The Committee agreed to table the ASP for designated member review after receipt of the revisions requested below. Dr. Bin Gao and [Redacted by agreement] were designated as the ACUC members to review the revised ASP.

[Redacted by agreement]

(b)(5)

- The following ASPs previously reviewed by a convened quorum were approved by designated member review:
  - i. Title: “Administration of Ketone Body Esters as a Protectant Against Radiation Exposure and Free Radical Damage,” Redacted by agreement Approved 1/27/2020.

- The following Category 1b amendments were approved by designated member review:
  - i. Title: “Alcohol, Liver Injury, and Regeneration,” [Redacted by agreement] (Amendment 32), Dr. [Redacted by agreement] Add fomepizole treatment. Approved 01/21/2020.
  - ii. Title: “Alcohol, Liver Injury, and Regeneration,” [Redacted by agreement] (Amendment 33), Dr. [Redacted by agreement] Add bupropion treatment. Approved 01/22/2020.
  - iii. Title: “Role of the Endocannabinoid System in Mice,” [Redacted by agreement] (Amendment 4), [Redacted by agreement] Add Nutra-Gel Diet for oral drug administration. Approved 2/3/2020.
  - iv. Title: “Chronic and acute actions of drugs of abuse on synaptic function and morphology,” [Redacted by agreement] (Amendment 57), [Redacted by agreement] Add room strains INSR and CIN-IR. Approved 2/4/2020.
  - v. Title: “Alcohol, Liver Injury, and Regeneration,” [Redacted by agreement] (Amendment 35), Dr. [Redacted by agreement] Add strain CCR5 KO. Approved 2/5/2020.
  - vi. Title: “Behavioral and Pharmacological Analysis of Genetically Modified Mice,” [Redacted by agreement] (Amendment 19), [Redacted by agreement] Add new AAVs. Approved 2/10/2020.
  - vii. Title: “Mechanistic studies on mitochondrial dysfunction, apoptosis and tissue damage caused by alcoholic and/or nonalcoholic substances,” [Redacted by agreement] (Amendment 21), [Redacted by agreement] Addition of a procedure for sub-chronic treatment with thioacetamide and a study on the protective effect of berberine on liver fibrosis (adding a new experimental compound and rat strain). Approved 2/10/2020.
- The following Category 3 administrative amendments were approved:
  - i. Title: “Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice,” [Redacted by agreement] (Amendment 2), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 01/23/2020.
  - ii. Title: “Behavioral and Pharmacological Analysis of Genetically Modified Mice,” [Redacted by agreement] (Amendment 21), [Redacted by agreement] Add offspring room strain Aldh1L1-cre/ERT2CNRORiboTag. Approved 1/24/2020.
  - iii. Title: “Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice,” [Redacted by agreement] (Amendment 1), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 1/27/2020.



- iv. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 55), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 1/28/2020.
  - v. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 56), [Redacted by agreement] Add offspring room strain ChAT-DAT-D2F. Approved 1/30/2020.
  - vi. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 34), Dr. [Redacted by agreement] Add offspring room strain CX3CR1ERTROSA26-EYFP. Approved 1/30/2020.
  - vii. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by agreement] (Amendment 3), [Redacted by agreement] Add special care instructions for water deprivation. Approved 2/3/2020.
  - viii. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 5), [Redacted by agreement] Add mouse strain NOD. Approved 2/10/2020.
- The following Animal Study Proposals underwent annual review:
    - i. Title: "Behavioral and Pharmacological Analysis of Genetically Modified Mice," [Redacted by agreement] Number of mice used as of 01/07/2020 – 4,389. Of the 4,389 animals used, 42 mortalities and 84 clinical cases were reported. 1,307 survival surgeries have been performed. There have been 21 amendments since this ASP was approved. Amendments 20 and 21 were approved during the annual review process and Amendment 19 was approved shortly after the annual review was completed. T&E forms have been reviewed for all animal users listed on the ASP that will use animals. Investigators performing procedures requiring demonstration of proficiency have demonstrated proficiency or have been notified that demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.

The next ACUC meeting is on February 25, 2020 at 1:30pm in [Redacted by agreement]

## NIAAA ACUC MEETING MINUTES

February 25, 2020

The NIAAA Animal Care and Use Committee (ACUC) convened on Tuesday, February 25, 2020 at 1:30 p.m., Redacted by agreement

### Attendance

#### Members:

<input checked="" type="checkbox"/>	Dr. Bin Gao	Chairperson, LLD
<input type="checkbox"/>	<span style="border: 1px solid black; padding: 0 20px;">Redacted by agreement</span>	
<input checked="" type="checkbox"/>	Dr. Raouf Kechrid	Attending Veterinarian, OLAS
<input checked="" type="checkbox"/>	<span style="border: 1px solid black; padding: 0 20px;">Redacted by agreement</span>	
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☒ Present   ☐ Absent

#### Guests:

Redacted by agreement

### 1) Old Business

- The committee reviewed and approved the January 29, 2020 ACUC meeting minutes as written.
- **Physical plant**
  - No new updates or developments to discuss at this time.

### 2) New Business

- **ACUC Policy Review**
  - **Administration of Agents that may induce Hypothermia:** The Committee performed the triennial review of the NIAAA ACUC Policy on Administration of Agents that may induce Hypothermia. No changes were made to the policy and none were suggested during review at the meeting. The policy was re-approved as written.
  - **Submission of ASPs and Amendments:** The Committee reviewed recent revisions that were made to the NIAAA ACUC Policy on Submission of ASPs and Amendments. The reference to SOP 3680 on page 3 was removed and replaced with

a reference to ASP OLAS-2, Rodent Holding Program. This new ASP effectively replaced SOP 3680 when it was approved on 12/17/2019. At the bottom of page 5, a sentence was added to clarify that administrative changes such as typos, grammatical corrections and contact information updates may be done without ACUC approved policies, consultations or notifications. The ACUC unanimously approved the changes.

- **Second Draft of NIAAA AAALAC PD submitted to OACU:** The Committee was informed that the second draft of the NIAAA AAALAC PD was submitted to the Office of Animal Care and Use (OACU) on February 13<sup>th</sup>, 2020. Comments should be received back from the OACU during the month of March, with final submission of our PD due in April 2020. The NIH AAALAC site visit has been scheduled for the week of June 15<sup>th</sup>, 2020. The site visitors should be touring our animal facility and auditing our animal use program in the afternoon of Thursday, June 18<sup>th</sup>, 2020.
- **ARAC Guideline Updates:** Revisions recently made to ARAC Guidelines listed below were presented to the NIAAA ACUC members as follows:
  - **Guidelines for Survival Rodent Surgery:** Most of the changes consisted of rewording and clarification of procedures. Definitions were updated and examples of major survival surgical procedures were included. The most significant changes were made to the 'Operative' section of the Guideline. Information regarding suture selection and different types of needles for wound closure was added. Recommendations for performing surgical procedures in series on multiple animals were also provided. A statement was added to indicate that post-operative monitoring of animals is required along with the creation and maintenance of surgical records. Table 3 was updated to specify that alcohol (ethanol or isopropanol) is neither a sterilant or high-level disinfectant.
  - **Guidelines for Collaborative Animal Studies:** Revisions made to this Guideline were mainly editorial and hyperlinks were updated as needed. Three models for collaborative animal studies are presented in this Guideline with Transfer of Ownership (Model 1) being the easiest. All three models were briefly presented to the NIAAA ACUC.
  - **Guidelines for Collecting and Releasing Animal Images and Audiorecordings:** This is a newly approved ARAC Guideline that details proper procedures for collecting and releasing of photographs, video and audio recordings of animals (alive and dead) in animal facilities and animal laboratories at the NIH. The NIAAA ACUC members actively discussed this new Guideline including the reasons for its creation and compliance with the Guideline.

### 3) Animal Study Proposals

- The following ASP was reviewed by Full Committee Review (FCR) at a convened meeting of a quorum:

- i. 

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(b)(5)

 The Committee



4/17/2020

agreed to table the ASP for designated member review after receipt of the revisions requested below. [Redacted by agreement] were designated as the ACUC members to review the revised ASP.

(b)(5)

(b)(5)



(b)(5)

- The following ASP previously reviewed by a convened quorum was approved by designated member review:
  - i. Title: “Mechanistic and translational studies on mitochondrial dysfunction, apoptosis and tissue damage caused by alcoholic and/or nonalcoholic substances,” [Redacted by [Redacted by [Redacted by]]] Approved 02/27/2020.
- The following Category 1a amendment previously reviewed by a convened quorum was approved by designated member review:
  - ii. Title: “Exploration of Brain Glycinergic and Glial Transmission in Mice,” [Redacted by [Redacted by [Redacted by]]] (Amendment 16), [Redacted by [Redacted by [Redacted by]]] Add two new models of neuropathic pain. Approved 04/08/2020.

- The following Category 1b amendments were approved by designated member review:

- i. Title: "Behavioral and Pharmacological Analysis of Genetically Modified Mice," [Redacted by agreement] (Amendment 22), [Redacted by agreement] Add strain S1-DAT-Cre. Approved 02/19/2020.
- ii. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by agreement] (Amendment 4), [Redacted by agreement] Add 6-OHDA intracranial injections. Approved 02/25/2020.
- iii. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 58), [Redacted by agreement] Add mouse Room Strain hs599CreER and Crl:CD1(ICR) and offspring room strain hs599-TdTom; add experimental compound tamoxifen and dosing by oral gavage. Approved 02/24/2020.
- iv. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 8), [Redacted by agreement] Allow for administration of the chemical hazard Saporin and its conjugates within the FLAC outside of a ducted BSC. Approved 02/28/2020.
- v. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 37), Dr. [Redacted by agreement] Add rotarod test. Approved 02/28/2020.
- vi. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 7), [Redacted by agreement] Addition of mouse Room Strain Ghsrla FLOX and associated offspring room strains. Approved 03/04/2020.
- vii. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 9), [Redacted by agreement] Add Room Strains mGluR5 KO, mGluR5loxP, Abhd14b KO, GPR132 KO, and Foxj1-CreERT and associated offspring room strains. Approved 03/04/2020.
- viii. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by agreement] (Amendment 5), [Redacted by agreement] Allow intracranial injection of 6-OHDA without the use of a ducted Class IIB biological safety cabinet. Approved 3/12/2020.
- ix. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 38), Dr. [Redacted by agreement] Add room strain CXCL1 KO. Approved 3/12/2020.
- x. Title: "Mechanisms involved in fetal alcohol exposure," [Redacted by agreement] (Amendment 2), [Redacted by agreement] Add ordering of timed pregnant dams and acute alcohol treatment experiments. Approved 3/18/2020.

- xi. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 36), Dr. [Redacted by agreement] Add Hepa1-6 cell line based orthotopic tumor mouse model of HCC. Approved 3/19/2020.
  - xii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 26), Dr. [Redacted by agreement] Add injection of adenovirus-Nfkbiz. Approved 4/1/2020.
  - xiii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 28), Dr. [Redacted by agreement] Add injection of adenovirus-Nqo1. Approved 4/1/2020.
  - xiv. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 6), [Redacted by agreement] Add Room Strain ihCD59 and offspring Room Strain SftpcCre-ERT2-ihCD59 and ILY toxin. Approved 4/8/2020.
- The following Category 3 administrative amendments were approved:
    - i. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 59), [Redacted by agreement] Add offspring room strain D1MORD1T. Approved 02/21/2020.
    - ii. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 60), [Redacted by agreement] Add offspring room strain ChAT-IR. Approved 03/04/2020.
    - iii. Title: "The Role of Polyunsaturated Fatty Acids in Neurodevelopment, Neuroprotection and Functional Recovery after Injury – Mouse Model," [Redacted by agreement] (Amendment 4), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 03/05/2020.
    - iv. Title: "Metabolism and Function of Polyunsaturated Fatty Acids (Rats)," [Redacted by agreement] (Amendment 2), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 03/05/2020.
    - v. Title: "Behavioral and Pharmacological Analysis of Genetically Modified Mice," [Redacted by agreement] (Amendment 23), [Redacted by agreement] Add strains PKSd-Cre and SOM-Flp (no breeding). Approved 03/09/2020.
    - vi. Title: "The Role of Polyunsaturated Fatty Acids in Neurodevelopment, Neuroprotection and Functional Recovery after Injury – Mouse Model," [Redacted by agreement] (Amendment 5), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 3/12/2020.
    - vii. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by agreement] (Amendment 7), [Redacted by agreement] Add offspring room strain RGS9DGLa. Approved 3/24/2020.



- viii. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 61), [Redacted by agreement] Add offspring room strain D1TD1C1b. Approved 3/24/2020.

- The following Animal Study Proposals underwent annual review:

i.

[Redacted]

[Redacted] is still pending.

[Redacted]

ii.

[Redacted]

[Redacted] are not approved on this ASP. [Redacted]

[Redacted]

demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.

iii.

[Redacted]

[Redacted] This pilot study report will be submitted for ACUC review and approval if additional experiments

[Redacted]

iv.

[Redacted]

4/17/2020

(b)(5)

I amendment is currently pending. (b)(5)

(b)(5) Investigators performing procedures requiring demonstration of proficiency have demonstrated proficiency or have been notified that demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.

The next ACUC meeting is on March 24, 2020 at 1:30pm in Redacted by agreement

## NIAAA ACUC MEETING MINUTES

April 28, 2020

The NIAAA Animal Care and Use Committee (ACUC) convened on Tuesday, April 28, 2020 at 1:30 p.m., via virtual WebEx meeting.

### Attendance

#### Members:

<input checked="" type="checkbox"/>	Dr. Bin Gao	Chairperson, LLD
<input checked="" type="checkbox"/>	Redacted by agreement	
<input checked="" type="checkbox"/>	Dr. Raouf Kechrid	Attending Veterinarian, OLAS
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☒ Present ☐ Absent

#### Guests:

Redacted by agreement

### 1) Old Business

- The committee reviewed and approved the February 25, 2020 ACUC meeting minutes as written.
- Redacted by agreement remains pending. A response to the letter from the ACUC regarding requested revisions has not yet been received.
- **Physical plant**
  - Redacted procedure room renovations have been completed and equipment from Redacted has been moved to this new location.
  - The door to room Redacted is broken and it is unable to be repaired. Replacement of the door will be needed and plans for this have already been put in place.

### 2) New Business

- **COVID-19 Pandemic impact on** Redacted by agreement **activity:** An update was provided to the Committee regarding animal care and use activities within the Redacted during the COVID-19 pandemic. There have been no COVID-19 cases reported among the Redacted staff. The husbandry staff has been split into two teams and the teams alternate working

in the facility every other day. This was done to minimize the number of staff within the [Redacted] at one time to prevent gathering of more than 10 people and to maintain social distancing of at least 6 feet. When staff are not working on-site in the facility, they are teleworking at home by reviewing [Redacted] documents, SOPs, training materials, etc. Only routine animal colony maintenance by the research staff is allowed. All maintenance activities must be approved by the Scientific Director prior to initiation. As of Friday, 4/24/20, there were 477 breeding cages within the [Redacted]. The NIAAA Office of Laboratory Animal Science (OLAS) also participates in a daily Animal Resource Team (ART) check-in led by the NIH Office of Animal Care and Use (OACU). During this call, members from all Institutes with animal programs discuss the current operating status and any new developments.

- OLAW Reportable Animal Incident:** The ACUC discussed a recent animal welfare incident that occurred within the [Redacted]. On March 16<sup>th</sup>, pest management reported to the acting Facility Manager of the [Redacted] that two mice were found dead in the live pest trap in an animal holding room. The Animal Program Director was subsequently notified, and an email was sent to all investigators with mice in this animal holding room requesting help to identify the two mice. The NIAAA ACUC Chair, Vice-Chair and Alternate Vice-Chair, and the Director of the NIH Office of Animal Care and Use were also informed that an incident investigation was under way. An investigator quickly reached out to indicate that two mice were noticed to be missing from one of his animal cages and they likely belonged to him. It is very likely that the mice were loose in the animal room for a few days before being found in the live pest trap and therefore, did not have access to food or water. No food was found in the stomach when necropsy was performed by the Facility Veterinarian. The responsible animal caretaker was retrained by facility management on how to properly perform live pest trap checks. The Animal Program Director retrained the responsible investigator on animal cage maintenance activities as described in the Investigator Orientation Handbook, specifically that the number of mice in the cage must match the number listed on the top animal card in the card holder. A memorandum to the NIH Institutional Official was drafted as a summary report of the incident and the steps taken to prevent future occurrences of similar incidents. The ACUC reviewed this memorandum and the conclusions from the investigation and approved re-training of the animal caretaker and investigator to prevent future occurrences of similar incidents. The committee agreed that the incident should be reported to the NIH Office of Animal Care and Use although it does appear to be an isolated incident and is not representative of continuing noncompliance with PHS Policy.
- Recent OLAW site visit discussion:** The ACUC discussed the recent Office of Laboratory Animal Welfare (OLAW) site visit to the NIH that took place from March 2<sup>nd</sup> – March 6<sup>th</sup>, 2020. The facility inspection of the [Redacted] and animal activity locations took place on Monday, March 2<sup>nd</sup>. No deficiencies were noted by the site visitors during this inspection. On Friday, March 6<sup>th</sup>, another site visitor came to inspect the NIAAA Animal Program documents and records such as Animal Study Proposals (ASPs), Standard Operating Procedures (SOPs), ACUC Policies, Handbooks, Disaster Plan, etc. No deficiencies were noted during this document review. A compiled list of OLAW questions asked to all NIH Institutes throughout the week was provided to the ACUC members. This may be a useful for review prior to the upcoming AAALAC site visit to the NIH. The ACUC was also informed that the NIH Animal Welfare Assurance document approved and signed by OLAW is available on the NIAAA

OLAS SharePoint site. The final OLAW site visit report was received by the OACU and portions of the report that specifically cited an Institute as being commendable or needing improvement were extracted from this report and distributed to the individual Institutes. The NIAAA Animal Program did not have any areas where needs for improvement were indicated. We did receive two commendations for our protocol pre-review process and excellent animal care information forms.

- **ACUC Policy Review**

- **Submission of ASPs and Amendments:** The Committee reviewed recent revisions that were made to the NIAAA ACUC Policy on Submission of ASPs and Amendments. Revisions to the Policy were made based on comments that were received by the NIH from OLAW during their March 2<sup>nd</sup> – March 6<sup>th</sup>, 2020 site visit. OLAW commented that the IC VVC Policies were not consistent with OLAW Guidance NOT-OD-14-126 or ARAC Guidelines Regarding Significant Changes to Animal Study Proposals. Specifically, OLAW noted that VVC Policies lacked listing of specific procedures and references deemed acceptable and approved by the ACUC. The section regarding Category 2 amendments (those that are verified by VVC) in our NIAAA ACUC Policy on Submission of ASPs and Amendments was modified based on this comment from OLAW. An amendment submitted for a change in duration, frequency, or number of procedures performed on an animal, for example, a change in the length of dosing for an already approved experimental compound can no longer be verified and incorporated into the approved ASP by VVC. The NIAAA ACUC has not established or approved any specific procedures or policies that can be referenced for these types of changes to be verified by VVC. The word ‘approve’ with respect to the VVC procedure was also replaced with ‘verify’ since it is important to note that the veterinarian is not conducting designated member review (DMR) on behalf of the ACUC, but is serving as a subject-matter expert to verify that compliance with the ACUC Policies and ARAC Guidelines, etc. are appropriate for the animals in these particular circumstances. The possible outcomes following ACUC review were condensed from 4 to 3. This is not a significant change since the second and third outcome were simply combined into one possible outcome indicating that an ASP or amendment may be tabled for review of modifications requested to secure approval either through full committee review (FCR) or DMR. The revised policy also clarifies that it is the ACUC Chair that designates the ACUC members responsible for designated member review. The ACUC unanimously approved the changes.

- **NIAAA Spring 2020 Semiannual Program Review**

- **Semiannual Report:** The ACUC reviewed the Spring 2020 Semiannual Report. While the [Redacted] and Animal Activity location inspections are typically done by at least two members of the ACUC, only one member performed the inspections for this semiannual report. This was done in accordance with OLAW Notice Number NOT-OD-20-088 and out of an abundance of caution during the COVID-19 pandemic. Only 1 minor deficiency was identified when inspecting the [Redacted]. A post-operative cage was found containing both an isopad and corncob bedding, which is not in compliance with the OLAS Rodent Survival Surgery Handbook. This finding was corrected the



same day it was identified, and the bedding was changed to corncob. Two minor deficiencies identified in an animal activity location during the Fall 2019 semiannual inspections remain unresolved. The completion dates for these deficiencies have been extended to 12/31/20. The expired certification dates of the biological safety cabinet and the downdraft table have been reported to the NIH Division of Occupational Health and Safety by the responsible investigator.

The Committee discussed the awarding of the new husbandry contract to FEFA, LLC. Based upon FEFA's technical abilities and realistic cost proposal in relation to the work to be performed, the Technical Evaluation Panel (TEP), the LARC IV Project Manager and the Contracting Officer recommended the award of the task order to FEFA, LLC. FEFA took over the animal care contract starting April 1<sup>st</sup>, 2020. The Committee also briefly reviewed other recent administrative and procedural program changes that have occurred over the past six months.

The Committee reviewed the ACUC-approved performance standard for extended cage change frequency. Consistent with efforts to minimize disruption to the animals' microenvironment, the NIAAA ACUC approved a facility-wide extended change frequency for filter tops, wire-bar lids and stainless steel feeders that may or may not be integral with the wire bar lids used on microisolation style caging as described within the NIAAA Investigator Orientation Handbook. Rodent filter tops, wire-bar lids, and stainless-steel feeders used on micro-isolation style caging may be changed monthly. Care is taken to ensure feed is available *ad libitum*, the interior cage surface remains free of visible moisture and feed pellets retain character with no evidence of mold growth.

The ACUC has also approved an additional exception for Innovive disposable caging. The exception allows changing cage bottoms of individually ventilated Innovive cages once every two weeks instead of the once a week standard procedure for cages on Tecniplast IVC racks, Lab Products IVC racks, and Static racks. The high pressure low velocity airflow design of the Innovive ventilated rack allows the disposable cages to achieve the Guide performance standard of maintaining an adequate microenvironment for longer than one week. Additionally, the disposable water bottles are changed once every two weeks when the cages contain two or fewer mice instead of the once a week standard procedure. Innocage® disposable water bottles are supplied with water acidified to a pH of 2.9. The volume of water contained within Innocage® disposable water bottles is more than sufficient for two mice for two weeks. The acidification minimizes any growth of bacteria within the bottle following contact with the cage occupant's oral flora.

The Committee voted to approve the Spring 2020 Semiannual Report.

- **AAALAC PD updates:** Comments on the NIAAA AAALAC PD were received back from OACU on March 12<sup>th</sup>, 2020. OLAS responded to these comments and sent the final version back to OACU on March 19<sup>th</sup>, 2020. Tracked changes made to the AAALAC PD following the Fall 2019 semiannual program review were presented in

the ACUC packet as part of the Spring 2020 semiannual program review. A summary of the significant changes was presented to the Committee. The Committee was also informed that the AAALAC site visit has been postponed. It will now be scheduled for some time in the Fall (October 2020).

- [Redacted by agreement], the former [Redacted] facility manager was replaced by [Redacted]. A description of his background and experience was also added.
  - The Laboratory of Molecular Physiology (LMP) was removed from the AAALAC PD as this lab has discontinued their animal use and decided not to renew their active ASP.
  - OLAS was added to represent their two active ASPs [Redacted by agreement] for sentinel monitoring and rodent holding).
  - The collaborative study with NIA for research done with non-human primates under ASP [Redacted by agreement] was added.
  - A brief description of what is meant by non-disposable safety equipment was added.
  - The description of circumstances and conditions where animals are housed in rooms outside of dedicated containment facilities was expanded to include procedures followed to ensure hazard containment. As written, there are only two ASPs that require the use of hazardous agents outside of dedicated containment facilities. Recently, two additional ASPs have also added the administration of chemical hazards without the use of a ducted biological safety cabinet. This response will be updated accordingly.
  - Revisions were made to the possible outcomes following ASP review to match the recent changes that were made to the ACUC Policy on Submission of ASPs and Amendments.
  - A brief description of how the ACUC may use pilot studies was added.
  - A response was added to address the responsibilities for monitoring animals for potential pain and distress and describe mechanisms in place to ensure that personnel have received appropriate species- and study-specific training.
  - The table of approved food/fluid restrictions listed on ASPs was updated with current information.
  - A better description of the Animal Facility Environmental Monitoring (AFEM) system was added.
  - The table of approved justifications listed on ASPs for single housing was updated with current information.
  - The description of methods to verify dishwater temperature was updated.
  - A table of the mouse and rat anesthesia and analgesia formularies used in the [Redacted] was added.
  - A list of all the locations where CO2 euthanasia may be performed within the [Redacted] was added and a list of all lab locations where euthanasia may also be performed was added.
  - The appendices are now complete, and have been incorporated into the AAALAC PD.
- **Status of** [Redacted by agreement] **ASP:** There is no longer an active Principal Investigator associated with approved ASPs [Redacted by agreement] According to the Scientific

Director, the work associated with these two ASPs will not be continued and both are to be archived at this time. ASP [Redacted by agreement] has not been signed into approval by the ACUC Chair, but a new Principal Investigator will be needed for this ASP if the work is to continue. The ACUC Chair indicated that he may be interested in assuming the Principal Investigator responsibilities for this ASP. He will review the ASP and study objectives and re-submit the ASP for Full Committee Review if the decision is to continue with this line of experimentation.

- **ARAC Guideline Updates:** Revisions recently made to ARAC Guidelines listed below were presented to the NIAAA ACUC members as follows:
  - **Guideline for Euthanasia of Rodents using Carbon Dioxide:** This Guideline was revised/reviewed and approved by the ARAC in October 2019. The AVMA Guidelines for the Euthanasia of Animals was recently revised and republished in 2020. These guidelines modified the procedures for euthanasia of rodents using carbon dioxide. The recommended chamber fill rate was increased from 10% to 30% of the chamber volume per minute. Corresponding changes were made to the ARAC Guideline for Euthanasia of Rodents using Carbon Dioxide to comply with the new AVMA Guidelines. Changes were also made to [Redacted by] SOP 4330 to reflect these new recommendations.
  - **Guideline for Diet Control in Laboratory Animals:** This Guideline was revised/reviewed and approved by the ARAC in October 2019. The changes in this Guideline were briefly presented and discussed by the ACUC members. Updated ARAC Guidelines are available on the OACU website and will be posted on the NIAAA OLAS SharePoint page.
  - **Guideline for General Species Environmental Enrichment:** This Guideline was revised/reviewed and approved by the ARAC in November 2019. The General Species Environmental Enrichment Guideline was reworded slightly to clarify intent and the types of enrichment were reordered. Occupational enrichment was moved ahead of sensory enrichment. This guideline also specifies that documentation of environmental enrichment programs is mandatory for dogs and non-human primates, and it is recommended for rodents.
    - **Appendix 1: Environmental Enrichment of Rodents:**  
This appendix was updated with changes to grammar and wording, but these revisions did not impact the content of the document. References were also updated.

### 3) Animal Study Proposals

- The following ASPs were reviewed by Full Committee Review (FCR) at a convened meeting of a quorum:
  - i. [Redacted by (b)(5)]  
[Redacted by (b)(5)] The Committee agreed to table the ASP for designated

5/18/2020

member review after receipt of the revisions requested below. [Redacted by agreement]  
and [Redacted by ] were designated as the ACUC members to review the revised ASP.

(b)(5)

5/18/2020

(b)(5)

ii.

(b)(5)

(b)(5) The Committee agreed to table the ASP for designated member review after receipt of the revisions requested below. Redacted by and Dr. Redacted by agreement were designated as the ACUC members to review the revised ASP.

(b)(5)

The next ACUC meeting is on May 26, 2020 at 1:30pm via virtual WebEx meeting.



## NIAAA ACUC MEETING MINUTES

May 26, 2020

The NIAAA Animal Care and Use Committee (ACUC) convened on Tuesday, May 26, 2020 at 1:30 p.m., via virtual WebEx meeting.

### Attendance

#### Members:

<input checked="" type="checkbox"/>	Dr. Bin Gao	Chairperson, LLD
<input checked="" type="checkbox"/>	Redacted by agreement	
<input checked="" type="checkbox"/>	Dr. Raouf Kechrid	Attending Veterinarian, OLAS
<input checked="" type="checkbox"/>	Redacted by agreement	
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☒ Present ☐ Absent

#### Guests:

Redacted by agreement
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### 1) Old Business

- The committee reviewed and approved the April 28, 2020 ACUC meeting minutes as written.
- Redacted by agreement responded to the PI letter following review of her ASP at the February 25<sup>th</sup>, 2020 ACUC meeting. The revised ASP has been approved by the designated reviewers, but the ASP still needs to be reviewed and approved by the Division of Radiation Safety (DRS). Approval from the Institutional Biosafety Committee (IBC) for work with the AAVs is also needed prior to final approval of the ASP.
- Redacted by agreement responded to both ACUC letters following review of her ASP renewals for Redacted by agreement at the April 28<sup>th</sup>, 2020 ACUC meeting. The revised ASPs were approved by the designated reviewers. Redacted by was signed and became active on 5/20/2020. Signatures are currently being collected for ACUC approval of ASP Redacted by.
- **Physical plant:** Washington Suburban Sanitary Commission (WSSC) is currently scheduled to perform their periodic pH monitoring for the building during the week of June 1<sup>st</sup>, 2020.
- **COVID-19 Pandemic impact on** Redacted by agreement **activity:** Dr. Raouf Kechrid reported that there continues to be a limited amount of activity in the Redacted as only maintenance activities are currently allowed. It has been more than 14 days since the last

reported positive COVID-19 case among the [Redacted] staff and no other staff members have developed or reported signs of infection. Starting on 4/7/2020 as part of the COVID-19 response, [Redacted] staff were placed on a rotating work schedule where most staff members began working one day onsite and one day offsite with at home assignments. Assignments to be done at home are provided and completion is verified by the Facility Manager. As the [Redacted] prepares for phase 1 of the return of investigators to the physical workspace, additional coordination of schedules will be necessary to ensure that that the [Redacted] is never more than 33% occupied and a 6 ft. distance can be maintained between individuals. Building contractors and essential employees, such as the animal care staff, will receive priority consideration. The use of procedure rooms will be limited to one person/surgeon per day and each procedure room may only be used every 48 hours to allow for proper decontamination following use. OLAS is looking into adding procedure room calendars to the OLAS SharePoint site as a method of reserving the procedure room space online. This would be available in addition to the procedure room calendars physically in place at the entrance to the rooms and could help investigators with scheduling their procedures. [Redacted by agreement] stated that Lab Chiefs were directed to submit their plans for the phased return of lab members to [Redacted by agreement] for consideration. Once the plans have been reviewed and approved, they will be sent to [Redacted by agreement] and then finally on to NIH Central Offices for final consideration and approval. Individuals placed into Group A could possibly begin returning to the physical workspace beginning the second week in June. This is dependent upon the continued decrease in positive COVID-19 cases reported in Montgomery County, Maryland and procurement of sufficient levels of personal protective equipment (PPE) for all building occupants. Face masks are currently the most difficult PPE item to obtain.

- **OLAW Response to reportable animal incident:** The OLAS received a response back from the Office of Laboratory Animal Welfare (OLAW) on May 15, 2020 regarding the recent NIAAA reportable animal incident that was reviewed by the ACUC on April 28, 2020. OLAW determined that the actions taken to resolve the issues and prevent recurrence were appropriate. This topic is closed.

## 2) New Business

- **ARAC Guideline Updates:** Revisions recently made to ARAC Guidelines listed below were presented to the NIAAA ACUC members as follows:
  - **Guidelines for Blood Collection in Mice and Rats:** This Guideline was revised/reviewed and approved by the ARAC in October 2019. The previous title for this Guideline was The Guidelines for Survival Bleeding of Mice and Rats. It contains information on various routes of blood collection in mice and rats. One purpose of this Guideline is to assist investigators in selection of the best method for blood collection. A list of factors to consider for selection of an appropriate blood collection technique is provided. This Guideline also aims to assist investigators in application of proper technique and provides basic recommendations for various routes of blood collection. All blood sampling (including technique, frequency, and volume) must be included in an approved Animal Study Proposal (ASP) or referred to in an ACUC approved/reviewed Standard Operating Procedure. It is the responsibility of both the

researcher and the ACUC to select/approve the techniques and procedures that result in the least pain and distress to the animal, while adequately addressing the needs of the experimental design. Training and experience of the phlebotomist in the chosen procedure are of paramount importance. Any exceptions to these guidelines, e.g. increase in blood volume or frequency of collections, or retro-orbital bleeding without use of topical anesthesia, or surgical cannulation, must be scientifically justified in the ASP.

The acceptable quantity and frequency of blood sampling is dependent on the circulating blood volume. Of the circulating blood volume, approximately 10% of the total volume can be safely removed every 2 to 4 weeks, 7.5% every 7 days, and 1% every 24 hours. A table is provided in the Guideline with sample blood collection ranges based on body weight and collection frequency.

- **Guidelines for ACUC Oversight of Animal Protocol Activities in Shared and Central Facilities:** This Guideline was revised/reviewed and approved by the ARAC in October 2019. Dr. Raouf Kechrid pointed out that the NIAAA does not currently house any animals in central or shared facilities, however, it's good to know that this guidance is available. The principal responsibility for monitoring animal activities in shared or central facilities lies with the lead Institute/Center (IC). User ACUCs are required to monitor the activities of their IC's investigators within shared or central facilities. Two members of the user ACUC shall perform on-site assessments of their animals and associated animal activities in shared or central facilities. Physical visits should occur at least semiannually. When an investigation results from actions/inactions by the facility staff or as a result of a facility related event, the lead IC ACUC, ORS ACUC, or ORF will assume primary responsibility for the investigation and resolution of the issue. When an investigation results from actions/inactions by an investigator or their staff, the PI's IC ACUC will assume primary responsibility for the investigation and resolution of the issue. The investigating ACUC will keep the other impacted ACUCs informed of the outcome of the investigation via direct communications and/or sharing copies of the draft and final summary memos.
- **Guidelines for Co-Housing Multiple Species of Laboratory Animals:** This Guideline was revised/reviewed and approved by the ARAC in November 2019. Dr. Raouf Kechrid mentioned that there is currently no co-housing of mice and rats in animal holding rooms within the [Redacted] As the demand for animal space within the [Redacted] continues to rise, co-housing of mice and rats in the future could be a possible solution. Given the potential negative impact on animal welfare associated with co-housing, efforts should be made to house mice and rats in separate rooms. If co-housing is necessary, it should be reviewed by the IC ACUC. If approved, mice and rats held in the same room should be housed in individually ventilated caging and consideration should be given to visual separation or barriers between the two species.

### 3) Animal Study Proposals

- The following ASP was reviewed by Full Committee Review (FCR) at a convened meeting of a quorum:

- i. (b)(5) The Committee agreed to table the ASP for designated member review after receipt of the revisions requested below. Redacted by and Dr. Bin Gao were designated as the ACUC members to review the revised ASP.

(b)(5)

- The following ASPs previously reviewed by a convened quorum were approved by designated member review:

- i. Title: "Metabolism and Function of Polyunsaturated Fatty Acids (Rats)," Redacted by Redacted by agreement Approved 05/20/2020.
- ii. Title: "The Role of Polyunsaturated Fatty Acids in Neurodevelopment, Neuroprotection and Functional Recovery after Injury – Mouse Model," Redacted by Redacted by agreement Approved 06/03/2020.



- The following Category 1b amendments were approved by designated member review:

- i. Title: "Metabolism and Function of Polyunsaturated Fatty Acids (Rats)," [Redacted by agreement] (Amendment 1), [Redacted by agreement] Add Special Care Instructions for Nonhazardous Water Additive and remove sucrose from the experimental compound table. Approved 6/2/2020.
- ii. Title: "Role of Endocannabinoids and Oxidative Stress in Injury of Heart, Liver, Kidney and Brain," [Redacted by agreement] (Amendment 30), [Redacted by agreement] Add new procedures for depletion of gut microbiota experiments. Approved 6/4/2020.
- iii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 39), Dr. [Redacted by agreement] Add new animal activity locations 2S-12 and 2S-30. Approved 6/10/2020.
- iv. Title: "The Role of Polyunsaturated Fatty Acids in Neurodevelopment, Neuroprotection and Functional Recovery after Injury – Mouse Model," [Redacted by agreement] (Amendment 1), [Redacted by agreement] Add three FLP recombinase knock-in mouse strains. Approved 6/19/2020.
- v. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 62), [Redacted by agreement] Add experimental compound diazepam. Approved 6/23/2020.
- vi. Title: "Chronic and acute actions of drugs of abuse on synaptic function and morphology," [Redacted by agreement] (Amendment 63), [Redacted by agreement] Add mouse room strain Drd2-Cre. Approved 6/23/2020.
- vii. Title: "Exploration of Brain Glycinergic and Glial Transmission in Mice," [Redacted by agreement] (Amendment 18), [Redacted by agreement] Add intrathecal viral microinjection in mice. Approved 6/26/2020.
- viii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 41), Dr. [Redacted by agreement] Add strains Ces1d KO and Ces1d f/f and associated offspring room strains. Approved 7/7/2020.
- ix. Title: "Role of Endocannabinoids and Oxidative Stress in Injury of Heart, Liver, Kidney and Brain," [Redacted by agreement] (Amendment 31), [Redacted by agreement] Add Tlr4 KO mice. Approved 7/8/2020.
- x. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 42), Dr. [Redacted by agreement] Add mouse strain miR-142 f/f, and offspring Room Strains LYZmiR-142, CD4CgmiR-142, ALBmiR-142, and LRATmiR-142. Approved 7/16/2020.
- xi. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 43), Dr. [Redacted by agreement] Add mouse strain BALB/cJ. Approved 7/16/2020.



- The following Category 3 administrative amendments were approved:
  - i. Title: “Alcohol, Liver Injury, and Regeneration,” [Redacted by agreement] (Amendment 40), Dr. [Redacted by agreement] Add offspring room strain E2aMIR-223. Approved 6/26/2020.
  - ii. Title: “Role of the Endocannabinoid System in Mice,” [Redacted by agreement] (Amendment 10), [Redacted by agreement] Add investigator [Redacted by agreement] Approved 7/15/2020.
- The following Animal Study Proposals underwent annual review:
  - i. Title: “Development and characterization of new probes to study the endocannabinoid [Redacted by agreement] Number of rats used as of 05/12/2020 – 0. There is no breeding or survival surgery approved on this ASP. There have been no amendments since this ASP was approved. T&E forms have been reviewed for all animal users listed on the ASP that will use animals. Investigators performing procedures requiring demonstration of proficiency have demonstrated proficiency or have been notified that demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.
  - ii. [Redacted by agreement] [Redacted by agreement] are not approved on this ASP. There have been 2 amendments since this ASP was approved. T&E forms have been reviewed for all animal users listed on the ASP that will use animals. Investigators performing procedures requiring demonstration of proficiency have demonstrated proficiency or have been notified that demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.

The next ACUC meeting is on June 30, 2020 at 1:30pm via virtual WebEx meeting.

## NIAAA ACUC MEETING MINUTES

July 28, 2020

The NIAAA Animal Care and Use Committee (ACUC) convened on Tuesday, July 28, 2020 at 1:30 p.m., via virtual WebEx meeting.

### Attendance

#### Members:

<input checked="" type="checkbox"/>	Dr. Bin Gao	Chairperson, LLD
<input checked="" type="checkbox"/>	Redacted by agreement	
<input checked="" type="checkbox"/>	Dr. Raouf Kechrid	Attending Veterinarian, OLAS
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☒ Present ☐ Absent

#### Guests:

Redacted by agreement

### 1) Old Business

- The committee reviewed and approved the May 26, 2020 ACUC meeting minutes as written.
- Physical plant:** Nothing to report.
- COVID-19 Pandemic impact on** Redacted by agreement **activity:** Dr. Raouf Kechrid reported that individuals designated in Group A and Group B of the NIH phased return to the physical workspace have now returned to the building. The Redacted staff continue to work in two teams on a rotating schedule with staff alternating days onsite and offsite with at home assignments. Onsite staff report to the Redacted at 6am and complete animal room husbandry activities by 11am. This allows investigators access to the animal rooms after 11am and enables 6-foot social distancing between individuals. If investigators require access to the animal rooms prior to 11am, they may enter briefly e.g. to retrieve cages and only two people may be present in the animal room at a time. Proper PPE is required to be worn within the Redacted and may not be worn outside of the animal facility. Face masks are required to be worn both inside and outside of the animal facility, however, face masks worn inside the animal facility may not be worn out. This is to prevent the spread of animal allergens. An email notification with this information was sent to all animal users and a sign will also be posted at the entrances to the animal facility as a reminder.

## 2) New Business

- **ARAC Guideline Updates:** Revisions recently made to ARAC Guidelines listed below were presented to the NIAAA ACUC members as follows:

- **Guidelines for Review and Approval of Animal Study Proposals and Significant Changes:** Revisions were made based on comments that were received from OLAW during the March 2020 Audit of the NIH Animal Welfare Assurance. OLAWs comments were as follows:

*The designated member review (DMR) subsequent to full committee review (FCR) ACUC Policy for several ICs does not describe the procedure or provide guidance for implementing the process in accordance with OLAW's guidance NOT-247 OD-09-035.*

*The ARAC Guideline on Review, Approval and Post Approval Monitoring of Animal Study Proposals Including Designated Member Review does not describe the three options available to the designated member following the review (i.e. approve, require modifications to secure approval or request full committee review of the research).*

As a response to these comments, the OACU formed an Intramural Research Program (IRP) subcommittee and reviewed the current ASP approval guidelines and incorporated the changes suggested by the OLAW Auditors to improve the Guideline. Revisions to this Guideline were approved by ARAC on 6/24/2020. This revised Guideline clarifies the process for FCR and DMR and the outcomes following each type of review. It also clarifies what specifically needs to be in place for the use of DMR. The current NIAAA ACUC Policy on Submission of ASPs and Significant Changes remains in compliance with this revised ARAC Guideline.

- **Guidelines Regarding Changes to Animal Study Proposals:** Revisions were made based on comments that were received from OLAW during the March 2020 Audit of the NIH Animal Welfare Assurance. OLAWs comments were as follows:

*VVC Policies were not consistent with OLAW guidance or ARAC Guidelines regarding significant changes. Many ACUCs' policies lacked specific procedures determined to be acceptable by the ACUC or specific references for the veterinarian to use to verify the requested change. In addition, a veterinarian or veterinarians should be designated by the ACUC and a method to document the consultation with the veterinarian should be developed to ensure the change is included in the protocol. These criteria should all be included in the VVC Policy and the policy must be approved by the ACUC.*

As a response to this comment, the OACU formed another subcommittee and reviewed the existing ARAC Guideline addressing Veterinary Verification and Consultation (VVC) practices and incorporated changes to clarify and correct deficiencies in the Guideline noted by the auditors. The revised Guideline was

reviewed and approved by the ARAC on June 24, 2020. Additionally, the subcommittee developed an example IC ACUC VVC Policy and both documents are posted on the OACU website. The OACU also intends to prepare a briefing on the VVC program for distribution to the ACUCs. The goal of this briefing will be to address the detailed requirements and procedures related to the VVC program.

The NIAAA VVC policy is outlined in the NIAAA ACUC Policy on Submission of ASPs and Amendments. It was modified recently based on these findings from OLAW, therefore the current Policy meets the expected standards.

- **Guidelines for Investigator-Managed, Small-Scale Zebrafish Satellite Facilities:** This Guideline was reviewed and approved by the ARAC on 6/24/2020. It is a new Guideline that was created as a response to comments that were received from the OLAW Audit of the NIH Animal Welfare Assurance in March 2020. When visiting the NINDS zebrafish satellite facility on [Redacted by agreement], OLAW expressed concern with the lack of separation between the zebrafish housing and the wet laboratory activities, which could put the health of the zebrafish and quality of the science at risk. The IRP proceeded to visit this particular satellite facility multiple times and concluded that the facility and program exceeds the minimum standards of the GUIDE and PHS Policy for the maintenance and use of zebrafish, specifically in regard to the training and experience required of the research and husbandry staffs, the requisite husbandry and water quality records, separation from laboratory activities necessary to prevent water contamination, and adequacy of emergency preparedness.

A team from the IC owning and directing this zebrafish satellite facility noted that no scientific equipment is in the room which could adversely affect the room's humidity levels, all electrical connections were raised off the floor, no volatile organic compounds were used in the room, and no pesticides have been applied in this area since the zebrafish colony moved to this location. The personnel supporting the zebrafish program are also well trained and experienced. The investigator who is also the primary caretaker of the fish system during the week has over 20 years of experience caring for zebrafish, and the [Redacted] rodent facility staff members who provide weekend and holiday care are trained by their contract managers in zebrafish husbandry. There were no animal welfare issues identified that would necessitate a move of the zebrafish facility and research laboratory to the Bethesda campus.

- **Guidance on ACUC meeting minutes:** Feedback was received from OLAW during the March 2020 audit of the NIH Animal Welfare Assurance regarding documentation of ACUC meeting minutes. OLAW commented that the *“ACUC minutes vary in the level of detail in the discussion of key functions of the ACUC, other than for protocol review or protocol amendment review. For example, semiannual program review and the associated discussions, unexpected deaths, animal welfare concerns, and review of ACUC policies were not documented”*.

As a response to this finding, an IRP subcommittee reviewed existing IRP guidance on ACUC minutes content and incorporated the guidance provided by the OLAW Auditors into an



‘ACUC Minutes Guidance’ document. The subcommittee is working on an example ACUC minutes format to accompany this Guidance document. These documents are intended to serve as a guide for individuals writing ACUC meeting minutes and a tool to improve the consistency of ACUC minutes throughout the IRP. Additionally, the OACU intends to prepare a short brief on this Guidance document to the ACUC Coordinators to explain the changes to the meeting minutes format and address why these changes were required.

It was noted that recusals from voting due to conflicts of interest should be documented in the ACUC meeting minutes. It is also best practice for those who recuse themselves to physically step out of the room during voting, and this will be strongly encouraged. A quorum of members must be maintained when a member is recused due to a conflict of interest.

- Summary of the IRP’s Responses to the March 2020 OLAW Audit Findings:** Dr. Kechrid reported that the OACU has been working on the response to the OLAW Audit Findings since the letter was sent to the NIH in April 2020. The final response is due to OLAW on 7/31/2020. In addition to the OLAW findings that were already discussed, Dr. Kechrid drew attention to a few other comments. The first concerned participation of the non-affiliate ACUC member in semiannual inspections. The auditors noticed that a few ICs did not have participation from the non-affiliate member for multiple, consecutive semiannual facility inspections. As these members are meant to represent the general community interests, their participation in these inspections should be encouraged. Another comment from OLAW concerned validation of the effectiveness of cleaning behavioral testing equipment. OLAW expects that this will be done semiannually. This will need to be discussed among the OLAS staff and the [Redacted] users in the near future to identify responsible individuals and determine a method for performing this type of monitoring. Dr. Kechrid also mentioned that the DOHS will begin annual facility and laboratory surveys and will be visiting the [Redacted] for an inspection soon. This inspection will be focused on occupational health and safety issues, and not necessarily concerned solely with animal welfare. These types of inspections have been done in the past, and will be done annually moving forward.

### 3) Animal Study Proposals

- The following ASP was reviewed by Full Committee Review (FCR) at a convened meeting of a quorum:

- i. [Redacted] (b)(5)  
[Redacted] (b)(5) The Committee agreed to table the ASP for designated member review after receipt of the revisions requested below. Dr. [Redacted] was recused during the vote. Dr. Bin Gao, [Redacted by agreement] [Redacted] were designated as the ACUC members to review the revised ASP. The modifications required to secure approval are as follows:

[Redacted] (b)(5)



(b)(5)



(b)(5)

- The following ASPs previously reviewed by a convened quorum were approved by designated member review:
  - i. Title: “Deciphering the mechanisms mediating the dichotomous effects of fever on brain function and behavior,” Redacted by agreement Approved 07/29/2020.

- ii. Title: "Chronic and acute actions of drugs of abuse on synaptic function and mouse behavior," [Redacted by agreement] Approved 9/2/2020.
- The following Category 1b amendments were approved by designated member review:
  - i. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by] (Amendment 6), [Redacted by agreement] Add diet intake analysis in Promethion food-monitoring cages. Approved 8/28/2020.
  - ii. Title: "Mechanistic studies on mitochondrial dysfunction, apoptosis and tissue damage caused by alcoholic and/or nonalcoholic substances," [Redacted by] (Amendment 1), [Redacted by]. Addition of two models of acute liver injury and usage of oral acetaminophen; add experimental compounds concanavalin A, D-galactosamine, and melatonin. Approved 9/1/2020.
  - iii. Title: "Exploration of Brain Glycinergic and Glial Transmissions in Mice," [Redacted] [Redacted] (Amendment 19), [Redacted by] Add Morris water maze and Y maze behavioral tests. Approved 9/1/2020.
- The following Category 2 amendment was verified by Veterinary Verification and Consultation (VVC):
  - i. Title: "Behavioral and Pharmacological Analysis of Genetically Modified Mice," [Redacted by] (Amendment 25), [Redacted by agreement] Modify surgical wound closure procedures for procedures requiring multiple survival surgeries (add wound clips). Approved 9/1/2020.
- The following Category 3 administrative amendments were approved:
  - i. Title: "Behavioral and Pharmacological Analysis of Genetically Modified Mice," [Redacted by] (Amendment 24), [Redacted by agreement] Add investigator [Redacted by] Approved 7/29/2020.
  - ii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by] (Amendment 44), Dr. [Redacted by agreement] Add offspring room strain CXCL1 KOB6J. Approved 8/12/2020.
  - iii. Title: "Behavioral, Pharmacological, and Electrophysiological Phenotyping of Genetically Modified Mice," [Redacted by] (Amendment 8), [Redacted by agreement] Add offspring room strain PvCreTdTom. Approved 8/12/2020.
  - iv. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 45), Dr. [Redacted by agreement] Add offspring room strain MRP8hCD59. Approved 8/13/2020.
  - v. Title: "Effects of dietary n-6 and n-3 polyunsaturated fatty acids on gene network in response to alcohol exposure," [Redacted by agreement] (Amendment 1), [Redacted by agreement] Add investigators [Redacted by agreement] Approved 8/27/2020.

- vi. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 12), [Redacted by agreement] Add new cross for Room Strain Foxj1-CreERT (backcross with C57BL/6J mice). Approved 9/1/2020.
  - vii. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] (Amendment 11), [Redacted by agreement] Add investigator [Redacted by agreement]. Approved 9/1/2020.
  - viii. Title: "Alcohol, Liver Injury, and Regeneration," [Redacted by agreement] (Amendment 46), Dr. [Redacted by agreement] Add offspring room strain ADIPOCgCes1d. Approved 9/8/2020.
  - ix. Title: "Deciphering the mechanisms mediating the dichotomous effects of fever on brain function and behavior," [Redacted by agreement] (Amendment 2), [Redacted by agreement]. Add Room Strains D1-TmtD2GFP, Emx1CreGAD67, GAD67FVB, PVCrehM3DqfxScn1afx, PVCrehM3DqfxScn1afxGAD67, PVCreTd-TomhM3DqfxScn1afxGAD67 and backcrossing of two strains. Approved 9/11/2020.
  - x. Title: "Chronic and acute actions of drugs of abuse on synaptic function and mouse behavior," [Redacted by agreement] (Amendment 1), [Redacted by agreement] Add investigator [Redacted by agreement]. Approved 9/14/2020.
  - xi. Title: "Chronic and acute actions of drugs of abuse on synaptic function and mouse behavior," [Redacted by agreement] (Amendment 2), [Redacted by agreement] Add investigator [Redacted by agreement]. Approved 9/14/2020.
- The following Animal Study Proposal underwent annual review:
    - i. Title: "Role of the Endocannabinoid System in Mice," [Redacted by agreement] Number of mice used as of 08/10/2020 – 5,099. Of the 5,099 animals used, 147 mortalities have been reported. There have also been 50 clinical cases reported and 0 survival surgeries have been performed. There have been 10 amendments since this ASP was approved. T&E forms have been reviewed for all animal users listed on the ASP that will use animals. Investigators performing procedures requiring demonstration of proficiency have demonstrated proficiency or have been notified that demonstration of proficiency is required. There are no pilot study reports to the ACUC that are pending.

The next ACUC meeting is on August 25, 2020 at 1:30pm via virtual WebEx meeting.