

University of Washington  
March 21<sup>st</sup>, 2024 IACUC Meeting Minutes

Members Present:	AB	GW	JS	MB
	BE	JFI	JT	MRB
	CC		KG	MK
				SF

Members Absent:	AP	DM	JPVH
	AW	GS	
		GL	

### Opening Business

- The Floor was opened for public comment at 2:30 pm.
- The IACUC Chair called the meeting to order at 2:36pm.

### Confirmation of a Quorum and Announcement

- Quorum was confirmed by JS.

### Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the February meeting minutes.  
Motion was made and seconded: to approve the minutes as written.  
Further Discussion: *none*  
Vote: Approved with 8 members voting in favor, 0 against and 4 abstentions.

### Benefit story:

Scientific research on cannabinoids has lagged even as more and more states legalize the use of medical and recreational marijuana. As more and more people turn to edible forms of the drug, it is important that we understand how this delivery route affects the rate and extent of distribution of THC and other active components throughout the body, especially the brain.

Most previous studies using rodents have given the drug through experimenter-delivered IP injection. While these studies have provided invaluable information, there are some key questions that they cannot address. These include effects of experimental treatments on voluntary consumption of cannabinoids and the bioavailability of active compounds that are orally ingested.

This month's Benefit Story is about the development of a mouse model for the voluntary oral ingestion of THC. The voluntary consumption of other drugs with the potential for abuse has been studied by dissolving the drug in gelatin, similar to 'Jello shots' for consuming alcohol. Unfortunately, rodents turn their noses up to gelatin mixed with higher concentrations of THC.

Three different UW labs participated in a collaborative effort to come up with a more palatable gelatin formula that could mask the aversive taste of the drug. They found that chocolate-flavored nutritional supplement, Ensure, achieved this goal without increasing consumption compared to a similarly sweet but

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non-chocolate flavored gelatin formula. This was crucial for getting rodents to voluntarily consume THC for studies looking at the effects of orally ingested drug on hypolocomotion, hypothermia and analgesia, all of which are classically affected by cannabinoids.

The researchers noted many similarities as well as a few differences in the effects of THC that was eaten compared to IP injections. Some interesting differences were also noted in the biokinetics of orally ingested THC. Future studies will be able to use this mouse model to provide clinically relevant insights into the voluntary consumption of marijuana.

English et al. "A preclinical model of THC edibles that produces high-dose cannabimimetic responses" eLife 2023.

### **Attending Veterinarian's Report – CC**

#### Adverse Events:

I have checked with the leadership at all sites and have no adverse events to report at this time.

#### Protocol Monitoring:

We currently have 26 protocols on enhanced veterinary monitoring. Of these 26 protocols, 18 of them were placed on monitoring proactively at the time of procedure approval to provide enhanced support during development or implementation of complex procedures. The other 8 were placed on monitoring following an unexpected outcome. Of the 26 protocols, 8 of them are currently performing the procedure for which they are on monitoring. All PIs on monitoring continue to work with their veterinary monitor.

### **OAW Director's Report – JFI**

**IACUC metrics** – IACUC metrics are in the meeting folder

Site visit poll – Reminder to please fill out the poll or respond to the email indicating that you are not available. OAW is hoping to have all responses received by Monday so we can move forward with scheduling.

#### SLU Sound Survey:

The IACUC, during its most recent semi-annual review of the animal care program, recommended that Environmental Health & Safety perform a sound level survey of zebrafish vivaria. In February a sound level survey was performed at the SLU zebrafish facility. The report is in Supporting Documents if you'd like to review it. The report has also been provided to the manager of that facility. To summarize, although hearing protection is not required based on the length of anticipated worker exposure in the space, personnel are recommended to wear hearing protection while working in these spaces. Hearing protection is recommended to be offered to personnel in these areas. In response to this sound level survey, the facility manager indicated that they plan to make hearing protection available in the facility in the near future.

#### **Response to Letters:**

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**4339-01** – At the February meeting, an incident was reported to the committee in which mice were used for oral gavage training. The use of animals for training was not approved on the protocol. The IACUC voted to send the PI a letter of reprimand, specifically requesting additional information about their processes for training new personnel, and processes for ensuring PI oversight of animal activities. The PI provided a lengthy response to the letter, which I will try to summarize. The PI thanked the committee for the constructive critiques and suggestions. The PI described that every new lab member is provided with a comprehensive list of online and in-person training requirements. After personnel have completed the required training, they are added to the IACUC protocol. Before commencing any animal procedures, lab personnel are required to review the protocol with the PI to ensure understanding, ensure that the individual can access the protocol, and determine if an amendment to the protocol is needed. If any additional hands-on training is required, the PI or an authorized senior lab member will supervise the new personnel to ensure competency. Continued training will be provided through regular check-ins and hands-on practice sessions, facilitated through bi-weekly lab meetings. The PI reviewed all of these processes with the lab at their January 2024 lab meeting, including the PI reiterating that PI approval is required prior to performing animal procedures to guarantee competency and compliance. The PI is also in contact with their OAW liaison to schedule an in-person training workshop that is mandatory for all lab personnel who may work with animals. The PI also mandated that all lab personnel that work with animals must re-take the mouse hands-on training lab through CLATR, with an emphasis on oral gavage training. At this point all personnel have either completed the training or are registered.

**FHL** – At the February meeting, a noncompliance was reported to the committee involving unapproved work with octopus at Friday Harbor Labs. The IACUC voted to send a letter of reprimand to the PI, who is also the Director of FHL, as well as to the two individuals involved in the incidents. The letter to the PI detailed several actions required by the committee, including retraining, establishment of enhanced oversight, and the PI must attend a future meeting of the committee. The letter also requested additional information about corrective actions. The PI responded to this letter, expressing regret for the situation, acknowledging deficiencies in oversight by FHL and by them as the PI, and indicating an understanding of the gravity of the situation. For corrective actions, the PI described that discretionary funds have been used to pay an FHL staff member to be an IACUC liaison / Lab Manager for animal care issues. While the time commitment is small, the PI notes the seasonal nature of the work so there will be periods of much higher time commitment, and periods with less time commitment. The duties of the new IACUC liaison include communicating with incoming researchers about regulatory requirements, being involved in IACUC and other site visits, being given view access to all FHL protocols in HoverBoard, and maintaining regular communication with OAW. In terms of attending a future meeting, the PI indicated that they can be available to attend the May meeting via zoom. Additional corrective actions include that they have updated their Researcher Application form to clarify the regulations around vertebrate and cephalopod work. At the close of the letter, the PI provided their assurance that this noncompliance did not result from a willful disregard for rules or disagreement with ethical standards, but rather from issues with communication.

Discussion: The committee would like to be informed on how the new FHL liaison will be trained. It was noted that the individual appointed as the FHL liaison is in a good position to know which animals are taken into FHL facilities and has experience in IACUC site visits at FHL.

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**Individual #1** – In response to the same event, a letter of reprimand was sent to the individual who actually collected the octopus. In their response to that letter, they apologized for their involvement in the noncompliance, and acknowledged the seriousness of the oversight. They indicated that they have decided to withdraw from live cephalopod research at FHL. Their graduate work is focused around non-cephalopod invertebrates. They concluded their response by expressing regret for the oversight and appreciation for the opportunity to learn from the experience.

**Individual #2** – A letter was also sent to the visiting scientist involved in this event. In their response, they apologized and took responsibility for the failure to adhere to regulations and expressed support for the new and evolving regulations around cephalopod use in research and education. They listed several corrective actions, including that they will no longer work with octopus at UW, they have retaken or are arranging to retake the required training courses, and they will work with FHL management to establish an archival space for onsite storage of IACUC-related logs that belong to non-UW visiting researchers so that such logs are available upon request. They concluded their letter by expressing appreciation for the effort of the IACUC and others have put in to enabling their research with cephalopods at FHL and apologizing for their failure to comply with regulations.

Discussion: We will work with the FHL director to schedule a discussion of these changes with the IACUC.

**Noncompliances:**

There are 3 noncompliances to report this month

**4290-01** - On January 24<sup>th</sup>, the group performed survival surgery on a rat, as approved in their IACUC protocol. The following day, while monitoring the rat, one of the surgeons noticed that one of the wound clips had come off and the wound was starting to dehisce. That individual replaced the wound clip themselves without consulting with veterinary services. The protocol at that time was not approved for a surgical repair procedure, and specifically stated that if wound dehiscence was observed they would contact veterinary services. The replaced wound clip fell off again by the following day, 1/26, and was not replaced. This incident was discovered incidentally 2 days later when a veterinarian, while following up on a different matter, noticed an animal with a partial wound dehiscence. At that time the animal was bright and alert, and the wound was clean and dry, so the veterinarian consulted with the group and advised monitoring the animal until its planned endpoint approximately 1 week later. The animal remained in good health until endpoint, and the rest of the rats in the 12-animal cohort also remained in good health with no dehiscence. The two individuals who performed the surgery had appropriate training through CLATR – one individual was certified to perform survival surgery in rodents, the other individual had completed the training courses and so was approved to perform surgery under direct supervision by a certified individual, as was the case. Upon being alerted to the noncompliance, the group immediately recognized and took responsibility for the noncompliance, and promptly submitted a self-report to their OAW liaison. The group

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also amended their protocol to allow them to perform a surgical repair if a wound clip falls out within 48 hours after surgery, and after consultation and approval by a veterinarian.

This has been reported to OLAW.

Discussion: The committee discussed the lab's experience with this surgery and the failure to immediately contact vet services.

Motion was made and seconded: to send a letter of counsel to the PI

Further Discussion: *none*

Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

**4375-01** - During a site visit on February 8<sup>th</sup>, the IACUC site visitors identified that a lab member that was present during the site visit, and who is also a certified surgeon for the group, was unclear about the difference between buprenorphine SR and buprenorphine HCl. As a reminder, buprenorphine SR, or sustained-release, provides 72 hours of analgesia after a single administration, whereas buprenorphine HCl, or hydrochloride, must be redosed every 8-12 hours. Upon further discussion with this individual it was discovered that this surgeon had been giving the mice a single dose of Buprenorphine HCl at the time of surgery rather than a single dose of Buprenorphine SR. This was a surgery that, per IACUC policy and their IACUC protocol, requires 48 hours of post-surgical analgesia. The individual indicated that, over the past year, he has misdosed 16 animals in this manner. They had not observed any signs of pain in these animals, and there are no records of any related sick animal reports. However, after being alerted to the issue, the surgeon did proactively review the mouse informational handout that CLATR provides and made note of the fact that pain can be difficult to assess in small rodents.

This is the only individual in the lab who is currently performing survival surgery. His training involved reading the protocol and performing practice surgeries with the PI. He was certified through CLATR in 2021. In response to this incident, the group is developing a checklist for surgeries to ensure that key steps are completed, and they are also revising their training procedures to ensure that an experienced lab member reviews the protocol with any new member, and initial survival surgeries performed by new members are supervised to ensure that, among other things, correct analgesia is administered.

This has been reported to OLAW.

Discussion: It was noted that this seems to have been an honest mistake. There was discussion about ways to improve education on this topic to prevent similar confusion in the future.

Motion was made and seconded: to send a letter of counsel to the PI with individual cc'd

Further Discussion: *none*

Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

**4317-01** – On February 27<sup>th</sup> a PI self-reported to OAW a protocol noncompliance involving administration of a substance via a route that was not approved on the protocol. This protocol is approved to administer

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protein nanoparticles to mice via SC, IM, and IP routes. In August of 2023, and again on February 21<sup>st</sup> 2024, a post-doc in the lab administered the nanoparticles IV via the tail vein. A total of 20 mice were involved, 10 in August and 10 recently. The August event did not come to the PI's attention because there were no adverse effects, but in the recent event the animals developed tail necrosis and were euthanized on 2/27 (the day of the report). The PI speculates that the difference in outcome may be due to the buffer, but that is unconfirmed. Last August the buffer was PBS, whereas in the recent event it was Tris/NaCl/glycerol.

The PI indicated that, at the time that the experiment was added to the protocol, there was confusion as to which routes should be included, and the intention was to include the IV route. The protocol is approved to administer other types of nanoparticles in other experiments via the tail vein route, so this is a route that is used by this research group. An amendment has been submitted to add IV administration to this experiment. Other corrective actions that the PI has already completed include a "read and understand" of the protocol with all members of the group, and the PI has also reviewed with all members the expectations around using HoverBoard as a resource to confirm what is approved.

This has been reported to OLAW.

Discussion: The committee discussed the impact of this event on animal welfare, possible root causes of the issue, and strategies for preventing similar occurrences in the future. It is not clear why these recent injections led to tail necrosis.

Motion was made and seconded: to send a letter of counsel to the PI

Further Discussion: *none*

Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

### **Standard Procedures / Policies / Guidelines - CC**

Last month, we discussed revisions that were made to the IACUC Policy for Surgery Training Requirements. Unfortunately, we did not record the vote for that item so we need to repeat that action today. It was included again in the supporting documents for your reference.

Changes to the policy included the following:

- Slightly revised the verbiage of the definitions of surgery and aseptic technique to match the definitions used in the Anesthesia Certification policy
- Clarified that CLATR coordinates surgery training
- Updated references from AUTS to CLATR and included links to the training requirements section of the CLATR website
- Added description of the content included within the surgery training coursework
- Removed the species breakdown for training requirements since the general topics of the training is the same regardless of species
- Removed the specific names of the courses provided by CLATR to allow for course title changes without amendments to the IACUC policy

Motion was made and seconded: to approve the policy as written.

Further Discussion: *none*

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Vote: Approved with 11 members voting in favor, 0 against, 1 abstention.

**Standard Procedures / Policies / Guidelines – AS**

8 blood collection and euthanasia procedures for mice and rats with no changes

Motion was made and seconded: to approve the standard procedures as written.

Further Discussion: *none*

Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

**Closing Business:**

The Meeting was brought to a close at 3:34 pm.