University of Washington
July 27, 2023 IACUC Meeting Minutes

Members Present:		ES		MRB
		GL		MS
	AP	JFI	MB	
	CC	JPVH	MK	
		JS		
	DT			
Members Absent:	DM	GS	KG	MRK
	AB			SP
	AW			

12 TOTAL

Opening Business

- The Floor was opened for public comment at 2:32 pm.
- The IACUC Chair called the meeting to order at 2:41 pm.

Confirmation of a Quorum and Announcement

- Quorum was confirmed by LM.

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the JUNE meeting minutes.
  Motion was made and seconded: to approve the minutes as written.
  Further Discussion: *none*
  Vote: Approved with 9 members voting in favor, 0 against and 3 abstentions.

Attending Veterinarian's Report – CC

I have checked with the leadership at all sites, and I have one reportable animal event for the committee at this time and one other update.

On 6/26/23, an adult male rhesus died while under anesthesia. The animal was on study and was under anesthesia for a procedure to debride around his cranial implant. Anesthesia was being performed by Veterinary Services. The animal was initially sedated with ketamine and then administered propofol for anesthesia (both of these are injectable agents). He was also intubated to protect the airway but was

breathing room air. Approximately 15 minutes after induction of anesthesia, the animal began to experience poor oxygenation (based on peripheral SpO2 monitoring) and a rapid, irregular heartbeat. Due to these vital signs, the veterinary technician requested to transition the animal to inhalant anesthesia with oxygen support. Another technician went to quickly retrieve a portable anesthesia machine to bring to the procedure space. The animal was attached to the anesthesia machine and immediately stopped breathing. A veterinarian was called, and the animal was taken to an area that has an anesthesia ventilator. Unfortunately, the animal went into cardiac arrest and was unable to be resuscitated.

Upon immediate review of the incident, it was identified that the portable anesthesia machine that was used was recently donated to Veterinary Services and had not previously been used. When it was initially grabbed from the storage space, it did not have a breathing circuit attached to it which was not noticed until taking the elevator to the animal procedure space. Due to the urgency of the situation, the technician leak-tested and pressure-tested the machine itself while someone else went to grab a circuit. The technician then attached the circuit to the machine and attached it to the animal. It was later discovered that this machine was not functioning properly with this type of circuit, and resulted in elevated pressures rapidly developing within the tubing.

Evidence of barotrauma was confirmed at gross necropsy confirming this increased pressure as the cause of death.

All staff involved were appropriately trained. All anesthetics and dosages used were verified to be correct. The anesthesia machine had been serviced by a commercial vendor within the required timeframe.

This machine has been removed from use and will be discarded.

Additional preventative measures being taken include:

- Leak and pressure checks must always be done with circuits attached
- To facilitate a more rapid emergency response, procedure spaces will be set up with emergency kits that include ambu bags and intubation supplies
- Any new or donated anesthesia machines will be fully evaluated by a veterinarian in addition to commercial vendor maintenance prior to use, and machines that are different from existing stock will require machine-specific training by all users prior to storage in any common-access storage area

This event occurred during our AAALAC visit and was reported to our site visit team while they were here. The team met with involved staff, reviewed surgical & anesthesia records, and reviewed our corrective/preventative actions. They acknowledged the unfortunate nature of the event but were complimentary of the emergency response by the vet staff and of our internal investigation and response to the incident. They were particularly impressed by the compassion of the staff involved as well as the compassion the PI exhibited to the staff following the incident.

This has been reported to USDA and OLAW as well.

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Update: Many of you may have heard about the intense heat wave in Arizona over the past few weeks. As such, we've been keeping a really close eye on our Arizona Breeding Colony, and I'm happy to report our systems continue to function appropriately. Our indoor rooms have been able to maintain temperatures within regulatory guidelines, and the animals are doing well. They are getting swimming pools and lots of frozen treats and seem to be tolerating the heat quite well.

Update on Protocol Monitoring: In the past month, we discontinued protocol monitoring for one protocol and did not add any new protocols for additional monitoring. Thus, we currently have 22 protocols with ongoing enhanced veterinary monitoring. Of these 22 protocols, 16 were placed on monitoring proactively at or near the time of protocol approval due to either the complexity of the project, at the request of the PI for veterinary collaboration, or due to the novelty of a specific procedure. The other six were placed on monitoring after the work began as a result of an unanticipated outcome. Of the 22 protocols, 8 are actively performing the procedure for which they are on monitoring. Those labs all continue to work closely with veterinary staff to carry out their work.

OAW Director's Report – JFI

IACUC metrics – IACUC metrics are in the meeting folder

Other Updates –

- Will send out site visitors with copies of concerns signs
- AAALAC Site Visit occurred June 22-30, preliminary findings included many commendations for staff and faculty as well as some identified areas for improvement. Findings will be finalized later this year. Reminder for DMRs- if you are an assigned reviewer and you cannot complete your review within the 1 week review period, to let OAW know as soon as possible so we can reassign.

Responses to Letters & Other Follow up –

2153-08– In May the IACUC voted to send a letter of counsel in response to a noncompliance in which 8 mice received a drug that was not approved for use in the study in which they were enrolled. In the letter, the IACUC asked to confirm that corrective actions reported to the committee had been implemented, including a double-check mechanism prior to initiating an experiment. The PI responded confirming that that they will make the procedural changes described in the letter.

Questions/Discussion: *The IACUC asked for a reminder of what was in the letter. There were drugs of a certain class approved, just not the specific drug, there were no adverse effects on animals. The lab responded as requested. No further action requested by the committee.*

4216-01 – In May the IACUC voted to send a letter of reprimand in response to a noncompliance in which survival surgeries were performed on mice without following the procedure as outlined in the protocol, including instrument and animal preparation and provision of post-operative analgesia. Also, while the surgeon had been trained internationally prior to joining UW, and had completed the surgery 1 and surgery 2 courses, they had not completed the required certification. In the letter the IACUC asked to confirm the corrective actions that had been implemented, and also asked for additional information about PI oversight as well as information about documentation of monitoring and post-procedural care. I will read the PI's response [letter was read].

Questions/Discussion: *The IACUC discussed that this lab has also been in touch with their Liaison as well. A member asked if the individual has completed their re-training. The IACUC will look into this and get back to them.*

4368-01 follow-up – In May the IACUC voted to send a follow-up letter to a PI regarding a noncompliance in which an investigator had mice that were beyond the age approved in the protocol, and had not been monitoring the mice as described in the protocol. This was originally reported in February, at which time the IACUC sent a letter of counsel. After discussing the PI's initial response at the May meeting, the IACUC voted to send a follow-up letter in which the committee requested additional information about methods and documentation for tracking and monitoring animals, and methods for ensuring protocol compliance. In their response, the PI acknowledged their responsibility for ensuring compliance with the protocol, and provided details about various types of data that are recorded, such birth date and weaning information, surgery date and notes, and post-operative monitoring. The PI also stated that "Animal activity... occurs according to our understanding of the IACUC protocol".

Questions/Discussion: *The IACUC raised concerns about the scope of the response. A member suggested that there need to be specific safeguards in place to prevent an incident such as this in the future, and that more frequent check-ins with the Scientific Liaison would be an appropriate measure. The IACUC requested that the Liaison closely follow this study in the future, and request a contingency plan if/when this study continues.*

4243-01 – In June the IACUC voted to send a letter of counsel in response to a noncompliance in which rabbits underwent an experiment that was not approved on the protocol. While all of the individual procedures were approved in different experiments on the protocol, they were not approved in the combination in which they were performed. The committee requested that the PI confirm the corrective measures that had been implemented. The PI responded, acknowledging the noncompliance, and confirmed they had reviewed the protocol and submitted an amendment to get the protocol in alignment with experimental plans. The group's two new lab members have also met with their OAW liaison to ensure that they understand the importance of following their IACUC protocol, as well as how to access and review their protocol in HoverBoard.

Questions/Discussion: *None, no further action requested by the committee.*

4045-02 – In June the IACUC voted to send a letter of counsel in response to an incident in which a researcher performed an unapproved repair surgery on an antelope ground squirrel, and also had not been following the wound closure techniques as approved in the protocol. In their response, the PI acknowledged the noncompliances, and described that they have met with the surgeon individually as well as with all personnel authorized to perform surgeries to remind everyone that they need to follow the IACUC protocol. Surgeries involving suture are paused until the approved type of suture is available, and they will consult with veterinary services to potentially give themselves more flexibility on the types of suture that can be used. The PI also stated that "any personnel performing surgeries will conduct more regular reviews of the IACUC protocol, improve their communication between research team members and veterinary staff, and will immediately consult veterinary staff for guidance if they have concerns about any step of the surgery procedure." The PI went on to state that they "will establish the practice that each time new personnel performs a surgery protocol, we will have a second person confirming that procedures are being performed in accordance with the protocol."

Questions/Discussion: *None, no further action requested by the committee.*

4154-01 – In June the IACUC voted to send a letter of counsel in response to a noncompliance in which mice were given a higher volume of vehicle than approved in the protocol. The PI responded, acknowledging and accepting responsibility for the noncompliance. As a corrective action, they have incorporated a protocol review session into the regular lab meetings, spending ~15 minutes at every-other-meeting focused on reviewing active experiments in the protocol. Frequency of these review sessions may decrease as all members become comfortable with reviewing the protocol in HoverBoard, but they plan to continue this practice at least once per month indefinitely. Other corrective actions include continuing to work with OAW and veterinary staff on building appropriate flexibility into their protocol, and emphasizing to all lab members the importance of reviewing the protocol prior to any experimental work, and bringing questions directly to the PI or senior lab staff.

Questions/Discussion: *None, no further action requested by the committee.*

Noncompliance –

3380-02 - On January 9th, a cohort of 5 mice underwent a blood draw and a skin biopsy followed by administration of one dose of buprenorphine. Following the biopsy, the mice were exposed to ultraviolet B (UVB) radiation, which is the radiation responsible for causing sunburns. UV exposure is known to precipitate symptoms in lupus patients, and this protocol studies the mechanisms for how that happens. Following the UVB exposure, the mice underwent a second blood collection and skin biopsy 24h later. The mice were reported to Vet Services for evaluation on January 10th. In conversation with Vet Services, it was discovered that the buprenorphine dilution that was used was expired. The expiration date listed on the dilution was 12/2022. This incident was promptly reported to the Attending Veterinarian, and the group self-reported this issue to OAW. The 5 mice were euthanized at scheduled endpoint on 1/11. There was no evidence of skin irritation or infection at the injection site or elsewhere at the time of euthanasia. This has been reported to OLAW.

Questions/Discussion: *The IACUC asked if the animals presented symptoms first before it was reported to Vet Services. It was clarified that the animals did not experience any clinical signs and it was reported to vet staff when they noted the date on the bottle. They also discussed that the solution was diluted. A member asked what they're going to do to better track expiration dates in the future. Other things that were discussed include that dilutions are prepared and labeled by Vet Services, and that the group should use a form to keep track of when solutions were prepared that they use to also log administration. The committee discussed sending a Letter of Counsel with recommendations discussed.*

Motion was made and seconded: to send a Letter of Counsel.
Further Discussion: *none*
Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

4489-01– On the dates of December 1st 2022 and March 6th 2023, approximately 20 mice total were euthanized with euthanasia solution that had expired in August 2022. This bottle of expired euthanasia solution, which was not labeled as expired, was found during an IACUC site visit of the lab space on February 21, 2023, and was noted as a finding during that visit. At the time of the visit the group was told to label and dispose of the expired bottle. Since this is a controlled substance, it must be disposed of through an authorized reverse distributor, so it could not be discarded at the time of the visit. The finding was formally entered in HoverBoard and sent to the group on March 1st, 2023. Note that the second date on which the expired euthanasia solution was used was on March 6th, five days after the finding was formally entered in HoverBoard and sent to the group.

On March 30th, 2022, the group formally entered a response in HoverBoard indicating that they were in contact with someone about disposal of the solution, and anticipated that it would be returned within the next few weeks. We considered the finding resolved at that time. However, during a visit of the space on June 27th, 2023, the expired bottle was still present.

OAW and the attending veterinarian have been in contact with the PI as we discuss the significance of the situation, potential impacts, and corrective actions. We have discussed with the PI that corrective actions may extend beyond just preventing recurrence in his lab but may also involve OAW and/or the IACUC adjusting their processes to prevent recurrence across the program. The PI has been responsive and forthcoming with all requested information, appears to understand the significance of the situation, and has accepted responsibility and expressed remorse. He has expressed willingness to work with OAW and the IACUC on any corrective actions suggested by the committee. Corrective actions already instituted by the PI include clearly labeling the bottle in question as expired, coordinating disposal of the drug, retraining lab staff, and limiting lock box access so only the PI can access controlled substances.

This has been reported to OLAW.

Questions/Discussion: *The IACUC discussed how the lab stores their expired products, and has recommended that they be kept separately in the same lock box. Other recommendations included keeping expired products in a separate plastic bag, labeled, with red tape on the vial to distinguish it. A member's suggestion was to have the IACUC purchase stickers for expired products and send them out with site visitors when they do inspections to use. A member questioned whether we can compel them to show their reverse distributor invoice. It was discussed that we cannot realistically implement this requirement across the board for the future but that it should be included in the letter for this case.*

It was discussed that this case was especially concerning since it had been noted at a prior site visit and considered resolved. There was concern that we need to be able to trust folks when they tell us they have done something, but in this case the specific individual didn't take the action required and agreed upon. It was further discussed that the PI's plan had been to report the findings at the next lab meeting but product was used in interim. Person who used the product is no longer in lab. The PI did report that staff are trained to check expiration dates and to not use expired substances. A question was asked about the number of active lab members, and lab is currently PI and one other person. It was noted that the PI has voluntarily paused all experimental work until they get an okay from the IACUC to proceed. There have been extensive meetings between OAW, AV, and this lab and the lab is taking it seriously. It was asked if they can use other methods to euthanize besides using solution, and this was unclear. Discussed sending a Letter of Reprimand. A member asked what the difference is in the letter types and it was explained that a letter of reprimand is considered more serious and there is a , distinction in tone of the letter.

> Motion was made and seconded: to send a Letter of Reprimand.
> Further Discussion: *include in letter: Instructions on how to separate a drug, how to document administration, provide reverse distributor invoice, describe new training program*
> Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

Protocol Review:

- Amendment to protocol 3108-04– **JFI**

- Reason for FCR: The group needs the amendment for a procedure planned for Tuesday morning 8/1.
- This amendment has been through OAW and veterinary pre-review.
- Background: The central focus of this protocol is to test the safety and efficacy of a new in vivo hematopoietic stem cell (HSC) transduction approach in non-human primates. Unlike current hematopoietic stem cell gene therapy approaches, this new approach does not require myeloablation and transplantation, but rather subcutaneous injections to mobilize HSCs from the bone marrow into the peripheral blood stream and then intravenous injection of a viral vector. This new approach could be clinically relevant for treating patients with severe hemoglobinopathies, like Sickle Cell Disease, or patients with HIV.
- Amendment: In this amendment the group is requesting to update the naming terminology of their vector to reflect their current vector strategy – this does not change the animal's experience on the protocol.
- They are also requesting to increase the maximum volume of blood that can be collected to greater than 10ml/kg/2 weeks during certain phases of the study while the animal is on tether. This would allow them to better monitor the animal's health as well as collect sufficient blood analysis. Hematocrit and hemoglobin will be monitored during this time, and collected volume will be decreased or blood collections will cease if hematocrit falls below certain values. Similar limits and justification are approved on other IACUC protocols.
- Lastly, several Standard Procedures in the protocol are being updated to new versions recently approved by the IACUC.

Questions/Discussion: *The IACUC clarified that blood collection limits are generally up to 10 ml/kg/2 weeks, they are requesting 13ml/kg/2 weeks, animal is a Macaque. A member identified that the animals on this protocol are being closely monitored. Questions included specifics of intervals.*

Motion was made and seconded: to approve the amendment as written.
Further Discussion: *none*
Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

Standard Operation Procedures / Policies / Guidelines- JFI

SOP's

- 918 Humane Endpoints – **JFI**

Motion was made and seconded: to approve the policy as written.
Further Discussion: *none*
Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

- 919E AIDS-related Monitoring Protocol – **JFI**
  last reviewed March 2020 and no changes

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

Further Discussion: *title is confusing with "protocol"; can approve with a suggestion for a name change from "protocol" to alternative*
Vote: Approved with 12 members voting in favor, 0 against, 0 abstentions.

Semi-Annual Report- BE

Report is attached to the meeting.

Questions/Discussion: IACUC members were recommended to read this report and incorporate it into their inspections.

IACUC Duties: to read Semi-Annual report, concur or not, report any concerns or questions, present a minority perspective. BE will send an email and they need to respond by concurring, disagreeing, presenting a minority perspective.

IACUC Training- STI

Postponed until next month or September.

Closing Business:
The Meeting was brought to a close at 3:44 pm.