University of Washington
November 16, 2017 IACUC Meeting Minutes

Members Present:			
	AB (Left at 4:24pm)	JFI	ML
	CG	JS	MS
	CH	JPVH	SH
	FRR	JM	SL
	JB	LJE	TB
		*MB	
Members Absent:	AS	JLS	PB
	KL		

* M.B alternate for AS

Other Business

- Response to Letter of Reprimand
  - *JS read excerpts from the letter of reprimand that was sent to the PI, and went through each concern and non-compliance, asking the PI to address each and explain how he is going to ensure that the non-compliances do not happen again. The PI said that they will have weekly lab meetings to cover requirements and that all personnel will be certified before performing surgery unsupervised.*
  - *Chair emphasized that another non-compliance could result in a suspension of the protocol.*

Protocol Review

- AMEND201701642 (3230-01) – **MB**
  - Briefly, the studies involve producing Traumatic Brain Injury in rats and then assessing the subsequent development of epilepsy and testing novel anti-epilepsy agents to prevent or treat the epilepsy.

    This amendment is being reviewed by the full committee because it is requesting an exception from *The Guide* and from the UW IACUC's policy on ***the use of post-surgical analgesics for pain control.*** No analgesia will be given post-injury because this research studies the chronic effects of traumatic brain injury, which is thought to be affected by analgesics. The IACUC needs to consider the welfare of the animals in the context of the researcher's scientific justification when considering this exception.

    Summary of this amendment:
    The fluid percussion injury (FPI) model is a very well established method of inducing reliable and reproducible experimental brain injury in rodents and it has been shown to reproduce many of the features of human traumatic brain injury (TBI). The overall goal of the laboratory is to assess the mechanisms responsible for the genesis and progression of post- traumatic epilepsy, which is a known and severe neurological complication of head injury. Physiological and electrophysiological experiments at the cellular, molecular, and in vivo level are required to understand the mechanisms of neuronal death and develop rational treatments. These studies are devoted to the development of acute and chronic treatments to prevent posttraumatic epileptogenesis.

    The research group now has two newly funded grants to continue this work by studying **EP2 (Prostaglandin) antagonists** as novel antiepileptogenic agents and **brivaracetam (BRV).**

The point of the proposed study is to assess the effect of these agents in this model to diminish the burden of chronic recurrent spontaneous seizures that develop after this brain injury. Brain inflammatory processes are thought to play an important role in epileptogenesis, and the development and frequency of seizures are critical endpoints. Thus any treatment that modulates inflammatory pathways has a strong potential to bias or invalidate these studies. In addition, anti-inflammatory agents that do not normally cross the blood-brain barrier cannot be used because fluid-percussion injury causes blood-brain barrier disruption, especially at the site of injury where the posttraumatic epileptic focus develops.

Conventional analgesic drug classes include opioids, NSAIDs, and local anesthetics. NSAIDs, Tylenol and opioids are all known to affect immune cells, inflammation, and the expression of a variety of inflammatory markers and mediators.

Motion: A motion was made and seconded to approve the amendment as written.
Discussion: *Even though the animals look good and a local analgesic is used at time of surgery, it is a major surgery, and it is reasonable to assume that there will be some pain/distress.*
There is swelling of the brain that occurs that likely causes pain, although seizures are subtle and aren't likely painful in this model. The approach that is being used in these studies is the same approach that has been used in the past, and is similar to the approach taken by other groups.

Vote on the Motion: The amendment was approved with 10 members voting in favor, 5 against, 1 abstention.

Other Business (continued)

- IACUC training on NHP socialization on WaNPRC – **JW**

Protocol Review (continued)

- PROTO201700034 (4158-10) – **JPVH**
    - The lab seeks to understand host immunity to Zika virus infection as well as identify, characterize, and develop effective antiviral immunotherapeutics and vaccines that target novel innate immune signaling pathways to potentially enhance immunity to control infections caused by Zika virus.

      Zika virus is an emerging virus that has recently caused a disease epidemic in Latin America. This outbreak has been labeled an emergency as Zika virus has sickened thousands of individuals worldwide, and of great concern, causes extreme birth defects. Indeed, nearly 4,000 children have been born in the last year with microcephaly attributed to Zika virus. This microcephaly (fetal brain injury) causes severe birth defects, and there is no prevention or cure at this time. Recently pigtail macaques have been developed as an animal model of Zika virus infection in which infants of mothers infected with Zika virus develop birth defects similar to those observed in humans after maternal infection with Zika virus. In this project the group

will use pigtail macaques as a model of Zika virus infection to study the immune response to infection and to develop new prevention and therapeutic strategies.

Reason for FCR:
This protocol has been called for a FCR due to a committee member's concern over how the group has reported findings of the Newman et al 2017 study and are using these findings to justify co-housing restrictions.

- *The group uses NHPs to develop a treatment for Zika virus.*
  The study is 13 weeks long and animals are to be restricted to grooming contact, instead of full body contact, for 28 days. The housing restriction at time of inoculation is requested due to the possibility of infection to other animals. It was suggested to separate animals for a few hours rather than completely.
  The primary mode of transmission of the Zika virus is mosquitos, but a common transmission is through sexual contact. This is why there is concern about vaginal secretions that could result in transfer of the Zika virus.

- *The risk of transferring the Zika virus by a bite is not known, but Zika can be transferred onto the skin, raising concerns about transmission with full contact when injuries are more common than with grooming contact.*

  Motion: A motion was made and seconded to approve the protocol as written with the co-housing exemption.
  Discussion: *Concerns were raised about transmission with grooming contact through saliva or skin exposure, or biting, but these risks are significantly lower with grooming contact compared to full contact. Injury rate with grooming contact is about 10%, but rises to 27% with full contact.*
  Vote on the Motion: The protocol was approved with 15 members voting in favor, and 1 against.

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the October 19, 2017 meeting minutes.

  Motion: A motion was made and seconded to approve the minutes as written.
  Discussion: None
  Vote on the Motion: The meeting minutes were approved with 12 members voting in favor and 4 abstentions.

Other Business (continued)

- Semiannual Report – **LI**
  - The IACUC reviewed deficiencies found during the past six months and discussed that they did not seem to indicate programmatic issues.

Standard Operation Procedures / Policies / Guidelines

- Significant Change Policy – **JFI**

  Motion: A motion was made and seconded to approve the policy.

Discussion: None
Vote on the Motion: The motion was approved with 15 members voting in favor and 1 abstention.

Member left at 4:24pm.

- Environmental Enrichment SOP for Rabbits **– TB**
  Motion: A motion was made and seconded to approve the SOP.
  Discussion: None
  Vote on the Motion: The motion was approved with 15 members voting in favor.

Protocol Review (continued)

- Repair Surgery 4316-01
  - This is a primate neuroscience protocol. The goal of this group's work is to better understand the neural mechanisms that underlie memory processes, and characterize neural signals that support memory formation.

    The group is requesting 1 repair surgery for animal number A13013, a 7 year old male rhesus macaque. His first surgery on this protocol was in August of 2014, when he received a head post implant. He had a chamber implanted in April of this year, and in August he had a craniotomy surgery followed 2 weeks later be surgical placement of a Microdrive. His repair surgery was used on October 26th to repair the Microdrive contacts, which was actually a non-surgical and non-sterile procedure but since it was not clinical and it required anesthesia, it was considered a repair. The group reports that the animal is otherwise healthy and there are no other current concerns with his implants. This animal is highly trained on multiple virtual reality tasks that he has learned over his past 3 years on this protocol.

    Based on his clinical history, he appears to be healthy, with good activity and appetite. He appears to have recovered well from his previous surgeries. His craniotomy surgery, which was performed in August, was initially planned for July but was delayed because exudate was found inside the chamber. The area was cleaned and debrided and the animal was put on antibiotic therapy. The craniotomy surgery proceeded in August without issue. Following implantation of his Microdrive in Mid-August, he was noted in his record to have weakness in his left hand. This resolved over the subsequent 2 weeks, with no concerns noted since then.

    Behaviorally, as noted in the request, this animal has minor to moderate alopecia and has exhibited infrequent potentially self-injurious over-grooming behavior, last observed in July. He is pair-housed with a long-term social partner and receives extra environmental enrichment as well as TV and audio enrichment.

  - *It was noted that the repair of the electrodes was made without making an incision into the skin or requiring additional sutures, and therefore is not technically a repair 'surgery', and is more appropriately termed a repair 'event', although it does require anesthesia. Repair events are not specifically included in the current protocol or in the current NHP policy on Neuroscience Studies. It was decided that this will be considered a repair surgery*

for the vote today, and that the current NHP policy/guidelines will be revised to include repair events.

Motion: A motion was made and seconded to have a sub-committee revise the Neuroscience Studies in Non-Human Primates policy to include repair events and bring the revision back to the IACUC.
Discussion: None
Vote on the motion: The motion was approved with 15 members voting in favor.

Motion: A motion was made and seconded to allow another repair surgery for A13013.
Discussion: None
Vote on the motion: The motion was approved with 15 members voting in favor.

Attending Veterinarian's Report - TB

- **Facility issues:**
  - **Humidity:** No issues reported.
  - **Temperature and lights:**
    - 10/22/17: Light cycles in one animal room did not turn on Sunday 10/22. The animal technician notified building maintenance and lights were returned to normal by Monday.
    - 11/13/17: SLU campus Lights did not turn off at night as they should have. Seimen's lighting system was at fault, they were contacted and got the problem resolved. On 11/14, on the rooms with an altered light cycle had the lights not come on. This was also fixed that day.
    - 11/13/17: Power surge with power outage cause the UPS on the Siemen's panel to fail on main campus resulted in lights in one animal facility containing multiple species not to come on in the morning as they should have.

- **Adverse event:**
  - **Protocol #: 4417-01**: 4 of 5 approximately one month old mice were found dead in a cage that was not fully engaged in the rack on 10/7/17. The remaining live mouse was dehydrated, thin and lethargic but recovered with fluid support. The group handled this cage the evening before the mice were found. The group member was very concerned about this event. The group member was retrained (10/13/17) on handling cages by AUTS in a one on one session. **This has been reported to OLAW.**
  - **Not Protocol Related:** On 8/20/17, a report was turned into vet services for six dead neonates in the cage, but the dam was also sick. The veterinary resident covering the facility that day did not understand that there was a sick animal to examine and thought all animals in the cage were dead, and did not look at the cage that day. The next morning, the remaining adult mouse was found dead. Necropsy revealed a uterine infection with two retained fetuses. The resident has been retrained as to how to interpret sick and dead animal reports. **This was reported to OLAW.**

OAW Director's Report – STI

- **Metrics are in the folder.**
- **Adverse Events**

- **Primate Center** Because of elevator malfunctions rooms 459 and 363 could not be changed out 11/14 and 11/15 - 2 day delay in change-outs for these rooms.
  - *The elevator is in need of total repair. This repair would require the elevator to be down for 9 months.*

  Motion: A motion was made and seconded to have the Primate Center inform the IACUC when the elevator will be repaired and report back to the IACUC in 2 months.
  Discussion: None
  Vote on the motion: The motion was approved with 15 members voting in favor.

- **Protocol 2174-23:** The goal of the program is to investigate the biology of aging and anti-aging intervention strategies using a variety of mouse models at older ages.
  Discrepancy in the currently approved protocol to administer doxorubicin (DOX) to mice one dose IV at 10 mg/kg in the substance administration, although in the experiment description it is listed as a single dose IP at 20mg/kg.
  Actual dose: Injected six mice 9 months of age with a 2 doses of DOX 10 days apart, both IP at 10 mg/kg. Although no adverse effects were seen physically or by echocardiography in the mice, this was clearly a procedure that had not been approved. This work was supported by an NIH grant.
  This incident was self-reported by the PI
  Follow-up: 1) The six mice are being held for observation, and no data will be used from them. 2) The PI is setting up a mandatory information session for new personnel coming on this protocol so that they understand that no procedure can be performed until approved. **This will be reported to OLAW.**
  Motion: A motion was made and seconded to send a letter of acknowledgment to the PI and group.
  Discussion: None
  Vote on the motion: The motion was approved with 15 members voting in favor.

- **Protocol 2326-08**: Z14362, a 2-year-old male Macaca nemestrina, was assigned to the project "Brain-computer interface for primates" (IACUC 2326-08) on 3/20/17. This project is approved for behavioral testing with food restriction. When animals are on controlled feeding, investigator staff feed the animals. When animals are not on controlled feeding, WaNPRC husbandry staff feed the animals. WaNPRC staff are trained not to feed animals that are marked "investigator feed" by a hanging sign on the animal cage and a procedure request posted on the animal room door.
  Z14362 was on investigator feed. On 8/18/17, there was a miscommunication between investigator staff and WaNPRC husbandry staff. A member of the investigator staff mentioned to a member of the WaNPRC BMS staff that the animal would be going off investigator feed. However, there was no written communication to the WaNPRC husbandry staff. The "investigator feed" sign remained on the animal room door, and the husbandry staff did not provide the animal with monkey chow. Food enrichment was provided and weekend feeding was provided as normal. Also, the animal has a social partner, and when the pair was reunited after mealtime Z14362 was able to eat his partner's leftover monkey chow.
  The problem was identified 10/4/17. A physical examination was performed immediately, and the animal was found to have lost some weight and had a lean body condition, but was

otherwise in good health. Full feed was restored. After the incident, the animal was monitored and followed and is doing well and in good health.

Corrective actions taken:

1. Feeding records of "investigator feed" animals are maintained by the investigator. These records had been maintained in the laboratory, but will now be maintained by the animal room to make it clearer to husbandry staff which animals are being fed by the investigator.
2. "Investigator feed" requests will need to be renewed monthly, rather than staying open-ended.
3. A "cheat sheet" of forms and procedures will be developed for investigator staff with clear instructions regarding who needs to be notified for different types of procedure requests and how they should be reported.

This will be reported to OLAW.

Motion: A motion was made and seconded to send a letter of counsel to the PI and the investigator requesting a response with a contingency plan to correct this issue in the future.
Discussion: None
Vote on the Motion: The motion was approved with 13 members voting in favor, 1 against, and 1 abstention.

- **Protocol 2013-01 – (LI):** This protocol uses various strains of transgenic mice to study the anti-tumor activity of T-cells. Nine cages of breeder mice were placed in packing boxes after 5pm the night before shipment and stored in the animal housing room until shipped at 9:30am the following morning. The mice had food and gel in the packing boxes. The lab member who packed the animals said they had contacted a commercial vendor for advice and had been told mice can be packed this way. When informed by Vet Services that keeping animals overnight in packing boxes is not an approved method of housing at the UW, she said they could find no IACUC policy or procedure about this issue, so contacted the commercial vendor for advice. The lab has agreed not to pack animals the night before shipping, but has still asked to see the IACUC policy that governs this.
  - *DCM has a 'How to ship animals' on their website that states that animals should be packed just before shipping, not the night before. DCM is putting together an FAQ.*

- **Protocol 2013-01 – (LI):** This issue was reported to the IACUC at the October meeting and the committee asked for further information. On 9/26/2017 a sick animal was reported to vet services. The vet tech and lab member examined the animal and agreed that it should be euthanized. However, when vet tech came back several hours later, the mouse had not been euthanized, the Vet Check card was not on the cage, and the lab member who reported the sick animal was gone. A vet came to re-examine the mouse, which died when he picked it up.

  Update: The lab member who agreed to euthanize the animal says she has no record of this incident nor does she remember it.
  The Vet Tech who reported the incident says no follow-up email was sent after the initial exam of this animal at 1:15 pm, since she had had the in-person conversation with the lab member.
  The Veterinarian says he looked at the mouse about 4:30pm; as he picked it up it died spontaneously in his hand. He says he called the lab and informed the lab member what had

happened. He says he may have left a voicemail, rather than talking to her in person, since he doesn't remember her reply.
In summary, the issue is that this lab member agreed with Vet Services to euthanize a mouse but did not do so.

Motion: A motion was made and seconded to a send letter of reprimand to this research scientist and the PI for non-compliances listed above for protocol 2013-01, asking for a written response explaining the steps being taken to ensure this won't happen again, in addition to making it very clear that any further instances could lead to suspension of the research scientist from research.
Discussion: None
Vote on the Motion: The motion was approved with 15 members voting in favor.

Closing Business:
The Meeting was brought to a close at 5:31pm. The floor was opened to public comment.