Members Present:  T. Brabb      S. Cunningham      R. Murnane
                A. Burich          C. Goodwin       J. Muster
                M. Byers           C. Grue           M. Newman (in late)
                C. Carrier         C. Hotchkiss    J. Stoloff
                E. Clark           M. Lucas         J. Sullivan
                J. Clark           L. Kinman        *M. Tetrick

Members Absent:  S. Brockerhoff    A. Leache          G. McLean
                 P. Lang

* M. Tetrick alternate for D. Fitts

Opening Business:

Dr. Cunningham called the meeting to order at 2:36 pm.

Protocol Review:

Opp, IACUC #4246-01 V.24 “Rodent Models of Central Nervous System - Immune System Interactions”

Dr. Brabb explained that Dr. Opp was present and available to answer any questions raised by the IACUC about his Significant Change request.

Dr. Brabb explained that the Significant Change was for the inclusion of studies that investigate the interactions between sleep disruption, inflammation, and the blood brain barrier transport as determinants of sepsis outcomes. For some of the studies he uses cecal ligation and puncture (CLP) which is a well-established model of sepsis. As part of this surgical procedure, a laparotomy incision is made and a defect is made in the cecal wall, which results in the development of peritonitis and sepsis.

The reason that this was brought to a Full Committee Review is that Dr. Opp is requesting approval to provide only 6 to 8 hours of pain relief postoperatively rather than 48 hours of pain relief, which would be in line with the typical analgesic guidelines. The change in pain relief would only apply to the CLP model and would not apply to the other surgical procedures approved as part of his protocol. This analgesic regimen was approved in his previous 3-year approval period.

Dr. Brabb explained that Dr. Opp was proposing this change because pain relievers, both NSAIDs and opioids have an effect on the brain, immune system and temperature regulation, which is what he is studying. In the sepsis studies, they strive for a balance of alleviating incisional and visceral pain associated with the procedure and the impact of the analgesic on critical outcome measurements.

Dr. Opp thanked the IACUC for the opportunity to discuss the Significant Change. Dr. Opp explained that in these studies they hypothesize that the brain responses to the septic insult are
critical determinants of outcome. This is important clinically because in a hospital setting sepsis remains the number one killer once someone is in the hospital. There are particularly bad outcomes for the elderly, which is why they are focusing on aging, the brain, and sleep disruption within the context of sepsis. In studying sepsis they have to be very careful about how they impact the brain before or during the development sepsis because they feel it would be very difficult if not impossible to separate the effects of buprenorphine from that of sepsis. Dr. Opp emphasized that they are trying to balance alleviation of pain and the impact of analgesics on outcome measures of interest.

Dr. Opp explained that there is not a lot of literature on the effects of buprenorphine on sleep but there are a lot of studies that demonstrate very profound effects of low dose buprenorphine on the EEG itself. There is more literature on the effect of buprenorphine on temperature regulation. Dr. Opp summarized the references that he had provided to the IACUC as part of the Significant Change request.

Mr. Kinman asked about how many animals would be involved in the modified analgesic plan. Dr. Opp said he didn’t have the exact number but estimated less than 100.

Dr. Hotchkiss asked about the endpoints of the study. Dr. Opp explained the monitoring protocol and endpoint criteria. If the animals survive beyond 72 hours they are considered survivors. Part of what the researchers are interested in is the effects of surviving sepsis so the survivors will be followed for quite some time.

Dr. Lucas asked how many animals had been used in the experiments that were done in the period of April through June 2013. Dr. Opp replied that they used about 120 animals in four groups, sham, CLP, adult mice and aged mice.

Dr. Cunningham asked how long the mice are followed once they reach the 72-hour time point. Dr. Opp replied they remain on the study for 30 to 60 days depending on what aspects of cognitive functioning they are looking at. Dr. Opp explained that these animals are cognitively impaired, and they are interested in that information.

Dr. Cunningham commented that there was data from human studies that reflect that same information and she asked Dr. Opp what was different about the work that he is doing. Dr. Opp replied that they have the potential with the mice to genetically target different systems within the brain that he thinks are important for these responses. They think that the temperature response and the sleep response to the septic insult are critical for determining ways to improve survival. They are in their second year of funding for research to manipulate brain systems by focusing on the brain rather than the periphery, which is the site of the insult, where 99% of the focus for all sepsis research is.

Dr. J. Clark asked how long after the insult they start their measures of interest. Dr. Opp replied that they are recording continually. Dr. J. Clark asked Dr. Opp to confirm that analgesics will be given prior to surgery and for up to 8 hours.

Dr. Grue asked if there was a policy change that was driving the review of the analgesic plan. Dr. Brabb replied that the policies about administration of analgesics had changed.
Dr. Thompson-Iritani asked if the group had any plans within the study to see if or how adding the pain medication would impact the results before the next 3-year approval cycle. Dr. Opp replied that it was a reasonable question that would depend on funding for those studies.

Dr. Carrier asked Dr. Opp about the mortality rate during that critical 72-hour period. Dr. Opp replied that there was 30% to 40% mortality. Dr. Carrier asked Dr. Opp to describe the monitoring protocol during the 72 hours period. Dr. Opp replied that they are monitored at least once a day. Dr. Carrier asked if there should be an increased frequency of monitoring. Dr. Opp proposed that they add one additional monitoring time point. Dr. Brabb confirmed with Dr. Opp that he would be willing to modify the significant change to indicate that CLP animals would be observed twice a day for the first 72 hours. Dr. Opp confirmed that he was willing to do that.

There were no other questions for Dr. Opp who thanked the Committee and left.

**Motion:** Dr. Brabb moved to approve the requested significant change with the addition of the 2\textsuperscript{nd} daily health monitoring of the animals during that first 72 hours, seconded by Dr. Sullivan.

**Discussion:** The Committee discussed the current literature and the possibility of a pilot study.

**Vote on the Motion:** The Significant Change was approved with 15 in members voting in favor, 1 member opposed and 1 abstention.

**Approval of the August 18, 2013 IACUC Meeting Minutes**

Dr. Cunningham called for a review of the August 18, 2013 Meeting Minutes.

**Motion:** Dr. Sullivan moved to approve the Minutes as written. Dr. Byers seconded the motion.

**Discussion:** none

**Vote on the Motion:** The minutes were approved with 13 members voting in favor and 4 abstentions.

**Attending Veterinarians Report**

**Facility Issues:**

- September 6, 2013 - Early in the morning there was a failure in the water management system at South Lake Union. Storm water backed up the sewer into the cage wash area of the SLU 3.1 animal facility and water entered the hallway and subsequently 4 animal rooms. No more than 2 inches of water was present in the animal rooms, and the facility personnel responded promptly to the issue. The long-term solution is to install a backflow-preventer on the sewer lines in 3.1. The part has been ordered and a site determined for installation.

- September 13, 2013 - A main water pipe broke in the Health Sciences Building. No damage was done to animal housing areas, but the water did have to be turned off for several hours (10:00 pm to 1:30 am) while the pipe was fixed. All animals were fine during this process.
Adverse Events:

- **Protocol #2183-02**
  Two male C57BL/6 wildtype mice born 7/2/2013 were found dead in a cage without food on 8/1/2013 (Thursday) by the animal care technician. They had been weaned with their littermates on 7/23/2013. On the afternoon of 7/29 (Monday), they were separated from their littermates by an individual in the investigators laboratory and placed into a new cage (presumably without food). The group did not have any further contact with this cage of mice and the animal technician did not change the cage. Necropsy and histology was consistent with the finding that these mice were housed without access to food.

  The animal technician in this room should have checked this cage on Tuesday morning and Wednesday morning, and discovered the error. The animal technician has been retrained, a letter has been placed in the technicians file and the facility supervisor is currently closely monitoring his work.

  Dr. Hotchkiss asked if there was a cage card on the new cage. Dr. Brabb replied that there was.

  Dr. Brabb commented that she wanted to try to determine how many times the animal technicians figure out that this type of event has happened and have corrected the situation. Dr. Brabb explained that there is an SOP that they follow when they find a cage without food. As part of this, a sick animal report is filed and veterinary services follows up with re-introduction of food to the affected animals. Dr. Brabb estimated that this happens at least once a month.

  Dr. Sullivan asked what communication there was to the person who moved the mice initially and failed to include food and also whether this might be a good time to look at the procedure for setting up new cages in order to prevent these types of events.

  Dr. Brabb replied that they are looking at the process and suggested that a process change such as already having food in the cages might work since they would then have to actively take the food out of the cage.

  Regarding the communication with the individual, the veterinarian on call talked to her and the PI. The person was a new graduate student and was mortified and very forthcoming about what happened, but thought that she had put food in the cage.

  Mr. Kinman asked what type of monitoring was being done for the animals as part of their protocol. Dr. Brabb replied the animals were just weaned and were not experimental animals and so were not on any specific monitoring protocol, however, the animal technician should have performed daily observations.

  **Motion:** Dr. Brabb moved to send the PI and the individual involved a letter of counsel asking for a reply addressing how they will prevent a reoccurrence of this type of event. Mr. Kinman seconded.

  **Discussion:** None
Vote on the Motion: The motion was approved unanimously with 17 members voting in favor.

OAW Director’s Report

Report on packets sent:

Since the last report at the August 15, 2013 meeting 3 packets and 7 e-mailed items have been sent to the IACUC. There were 7 new protocols. There were 54 renewals, of which 9 were three-year renewals requiring a complete Project Review Form. There were 45 annual renewals. There were also 93 Significant and Minor Changes. The IACUC has completed its approval process for many of these items, though some are awaiting final approval due to holds for items such as EH&S approval, OH review or signatures, or revisions from PIs.

Reply from Researcher Regarding Non-compliance Previously Reported:

At the August 15, 2013 IACUC meeting, the Committee was informed that unauthorized behavioral experiments were performed using 32 rats. It was explained that these experiments, previously were approved on the protocol, but were inadvertently left off of the protocol at the time of the 3-year renewal (June 2012) and the omission was not noted by either the PI or the student involved.

Based on the seriousness of the current event which resulted in wasted animals and data that could not be used for publication or grant proposals, the Committee voted to send the PI a letter of reprimand emphasizing the importance of following the approved protocol. The Committee requested a reply summarizing the practices that have been put into place to prevent future occurrences. The PI responded as requested and noted several changes to ensure that experiments previously approved on protocols will not be inadvertently left off at the time of the 3-year renewal:

The “Reminder: Protocol Due to Expire soon…” email from the OAW to the PI will be forwarded by the PI to ALL laboratory personnel, i.e., postdoc(s), graduate student(s).

The PI will access the protocol from the ‘Catalyst’ webpage.

Each lab personnel will be asked to update their current and planned experiments so that the PI can include them into the IACUC PRF (Project-Review-Form).

A spreadsheet of protocol experiment (KimLab) will be kept in ‘CLOUD’ (SkyDrive) and accessible to ALL lab personnel in real-time.

Reply from Researcher Regarding Non-compliance Previously Reported:

Also at the August 15, 2013 IACUC meeting, the Committee was informed about a situation in which a cohort of mice were used in a complicated series of behavioral experiments utilizing limit feeding and then food rewards for tasks. As part of these experiments, different individual animals/cages were removed from limit feeding at different times during the experiment.

On July 9, 2013, the post-doctoral fellow running the experiment made a mistake when removing one cage from limit feeding, such that the sign saying, “Investigator Will Feed” was left on the
cage and the cage was not given food. Six days later, one mouse was reported dead and the other sick. When the post-doc examined his records, he realized he had made a mistake with this cage and had not removed it from limit feeding as intended.

The Committee was informed that Dr. Brabb had spoken with the PI, the post-doc, and the facility manager regarding additional safeguards to be put in place to prevent a reoccurrence of this type of event.

The Committee voted to send the PI a letter of counsel and to request a written summary of additional practices that were put in place in order to prevent future occurrences of this nature. The PI responded as requested and noted several changes as follows:

The incident was discussed with Dr. Brabb and the individual responsible for the care of the animals in question.

The group instituted a new policy to safeguard animals under supervised calorie restriction: They now have a dedicated staff member who will oversee all experimental animals under calorie restriction.

All body weights that are recorded each day while under a “Special Service Request” will be confirmed “reported” by the dedicated staff members.

All body weight sheets will remain in the housing facility along with a color-coding system (a matching sticker placed on the weight sheet and cage card) to allow animal technicians to more easily identify animals that are actively calorie restricted.

Facility Extension Requests

Site Visit Deficiency Completion Deadline Extension Requests:

Dr. E. Clark informed the IACUC that there were two extension requests as follows:

- Site: Health Sciences H225A, H227, H231, J083B
  - Deficiency: Emergency power source is not available.

  Original Citation: 4/18/13
  Original Deadline: 9/30/13
  Extension Deadline: 12/31/13

  Reason for request: Rooms H225A, H227, H231, J083B do not have an emergency power source in case of a black out. Facility Services is requesting an extension for the project to 12/31/13 to allow the engineers’ time to plan and coordinate the emergency power for the labs that house zebra fish.

  Motion: Dr. E. Clark moved to approve the deadline extension request. Dr. Brabb seconded the motion.

  Discussion: none

  Vote on the Motion: The motion passed unanimously with 17 members voting in favor.
Site: Brotman 423
Deficiency: One pressurized gas tank secured with only one strap. Cylinders must be secured with a second strap or chain.

Original Citation: 8/7/13
Original Deadline: 9/16/13
Extension Deadline: 10/31/13
Revised Extension Deadline: 10/18/13

Reason for request: Ron Seifert is requesting an extension for installing a second strap to secure the gas tank in Brotman 423. He has submitted a work request through the Infocenter system, but the request has now changed to McKinstry (SLU maintenance). He has not received a response from McKinstry and will contact Mike Robertson, the Site Facility Manager for assistance. As a result, Ron is requesting that the deadline be extended to October 31, 2013.

Motion: Dr. E. Clark moved to approve the deadline extension request. Dr. Byers seconded the motion.

Discussion: Dr. Hotchkiss asked if the lab manager had actually talked to McKinstry as she felt they were very responsive. Dr. E. Clark replied that he had called them but had not received a response. Mr. Muster thought that McKinstry was usually very responsive and wondered if there was another issue here. Dr. Sullivan suggested approving a shorter extension because it should not take until the end of the month to complete the work.

Amended Motion: Dr. E. Clark moved to approve a deadline of October 18, 2013 for the repair. Dr. Byers seconded the motion.

Vote on the Motion: The revised deadline was approved unanimously with 17 members voting in favor.

Cage Height Variance – WaNPRC

Dr. Hotchkiss explained that the request was for an exemption to house infant monkeys (age 2 weeks to a body weight of 1 kg) in cages that meet floor space requirements but are only 24" high. These animals climb up well, but are not adept at climbing down. The lower cage height reduces the risk of injury if an animal should fall.

Motion: Dr. Hotchkiss moved to approve the variance. Dr. Grue seconded the motion.

Discussion: None.

Vote on the Motion: The cage height variance was approved unanimously with 17 members voting in favor.

[Dr. Newman arrived at the meeting at 3:31pm following the vote on the cage height variance.]
Standard Operating Procedures, Policies and Guidelines:

Dr. Brabb reminded the Committee that the SOPs for environment enrichment are being updated once a year in response to the new guidelines. This batch of EECs had not been changed since the Committee reviewed them last year.

Dr. Sullivan commented on the approved music. On a site visit the nature sounds that she heard being played in the pig room included wolf howls, which would be disturbing to the pigs. Dr. Sullivan suggested that with the use of nature sounds, there is a risk of the inclusion of sounds that are not appropriate for certain species. Dr. Brabb was agreeable to taking the forest sounds out of the SOP.

Dr. Thompson-Iritani asked how the enrichment is reviewed. Dr. Brabb explained that there is an enrichment committee that reviews the recommendations. Dr. Brabb said that she would ask the enrichment committee to review the use of Forrest Sounds.

Ms. Stoloff commented that the SOP for dogs indicates 10 minutes a day, four times per week and asked if there was any way to enlist volunteers in order to allow more exercise time for the dogs. Dr. Brabb explained that in the past, volunteers have been used. Dr. Brabb clarified that the policy is straight from the Animal Welfare Act and indicates only the minimum amount of exercise for animals that are housed in cages; most of the dogs are housed in groups. Ms. Goodman asked if the dogs have some contact with humans on weekends. Dr. Brabb confirmed that they do.

Motion: Dr. Brabb moved to approve the Environmental Enrichment Policies. Dr. E. Clark seconded the motion.

Discussion: None.

Vote on the motion: The motion passed unanimously with 18 members voting in favor.

Complaint to the IACUC:

Dr. Cunningham summarized a letter sent to the IACUC from Dr. Pippin asking the IACUC to reconsider Dr. Copass’ protocol and withdraw approval. Dr. Byers asked if Dr. Copass should be invited to a meeting if the Committee was going to consider withdrawing approval. Dr. Cunningham replied that if the Committee decided that they wanted to reconsider the approval of his protocol that he would be invited to attend the meeting. Dr. Grue commented that when the IACUC reviewed Dr. Pippen’s last request, both parties were present and were allowed to speak before the IACUC voted to approve the protocol.

Motion: Dr. Grue moved that the Committee respond to Dr. Pippin that the protocol was scheduled for renewal 9/15/14 and at that time the Committee will revisit the approval of the protocol. Dr. E. Clark seconded the motion.

Discussion: none

Vote on the Motion: The motion passed unanimously with 18 members voting in favor.
Sub Committee Updates:

• Pilot Project Review Forms

Dr. Istvan reported on the Pilot for the Project Review Form. There have been 5 completed forms and 3 have already gone out to the Committee. There are 7 groups committed to trying the forms for its development and there is a good distribution from the University community including Children’s and there have been some from radiology, physiology, medical genetics, comparative medicine, urology, and environmental and occupational health. They are so far weighted towards rodents and there is one pig protocol. There is a need for protocols using non-human primates, aquatics and fish, and he hopes to get some involving field research. There has been one technical glitch with an embedded spreadsheet, which is being addressed. Dr. Istvan reminded the Committee he would appreciate any comments or suggestions as people review these pilot forms.

• Nonhuman Primate Protocol Reassignment

Dr. Newman reported that the subcommittee met on September 13, 2013. They had a good discussion and she is working on setting up the next meeting.

• Site Visit Guidance Document

Dr. E. Clark reported that the subcommittee met on September 9, 2013. The 12 members broke up into smaller working groups and a follow up meeting is scheduled for September 30, 2013

IACUC Training:

Mr. Tetrick commented that on site visits it became apparent that there were different perspectives on the requirement for CO₂ flow meters. Some site visitors were noting this as a deficiency and others were just notifying the groups about the new policy. It was clarified that this should be noted as a deficiency.

Closing Business:

The meeting was brought to a close at 3:55 pm. The floor was opened to public comment.