

Meeting Date: November 15, 2007

Members Present:	J. Angelosante	D. Fitts	R. Marnane
	S. Cunningham	G. McLean	L. Hajjar
	N. Phillips	D. Lee	V. Batterson
	M. Slosberg	S. Skerrett	T. Brabb

Members Absent:	J. Kauffman	W. Dickhoff
	I. Washington	P. Fink
	S. Kelley	

Opening Business:

Dr. Cunningham called the meeting to order at 2:37pm. Dr. Cunningham explained that the meeting minutes would be reviewed following review of the protocols in order to accommodate the researchers present to support their projects.

Protocol Review:

❖ IACUC #3382-03 "Latent Mortality in Chinook Salmon from the Snake and Columbia Rivers" - Dr. Anderson

Dr. Brabb explained that the purpose of the protocol is to try and understand why juvenile Chinook salmon that are transported around dams have a lower smolt to adult return rates. The goals specifically are to determine survival curves and vitality parameters to model survival rates of transported and in-river juvenile to adult Chinook. Secondly, the investigators hope to determine if seasonality affects survival of transported salmon (spring versus summer).

One main issue was raised by the IACUC reviewers: The investigators planned to not feed the fish and then use death as an endpoint.

In response to these concerns, the Investigator proposed two pilot studies: In the first study, they will use Rainbow Trout compare calorimetry data obtained from fish that are maintained without food and an "increased water temperature" until they lose buoyancy to those that die. They believe that the loss in buoyancy will be a good biomarker for impending death and thus can then be used in their main study as an endpoint. They are using Rainbow Trout in this study because Chinook are out to sea and are not available for use.

The second pilot study will be to perform a time course of calorimetry changes over an approximate 20 day period.

Fish experience negative energy balance for a number of reasons in the wild, such as during migration and over the winter. Dr. Brabb explained that these are short term studies. The study is not intended to be a starvation study. Chinook Salmon naturally do not eat during the winter, and often don't eat during migration.

Discussion:

Dr. Cunningham Susanna asked if once the fish loose buoyancy will they be euthanized, or can they recover and would they eat? The PI explained that if they did recover, they would not be very healthy once buoyancy has been lost. Dr. Phillips confirmed that if a surrogate end cannot be determined as a result of the pilot study than the Committee is approving death as an endpoint. Dr. Batterson asked

how many animals would be used for these pilots. A member of the research team replied that in the Pilot Project 1, they will use 200 fish, of which, 20 will be euthanized prior to the challenge, 90 fish will be euthanized once the exhibit buoyancy problems and 90 fish will be allowed to die. For the second pilot project, 840 fish will be used, of which, 84 will be euthanized prior to the challenge and the remaining fish will be euthanized every 2 days for the rest of the 9 sub-samples (84 fish per time-point).

Motion: Dr. Brabb moved for approval of the protocol as written. Dr. Murnane seconded the motion.

Discussion Regarding the Motion: None.

Vote on the Motion: This motion passed unanimously with 11 members voting in favor. Mr. Slosberg was not present for the vote.

❖ IACUC # 2062-01 "Saccadic Eye Movement Studies" - Dr. Kaneko

Dr. Phillips explained that the Significant Change request is for an additional clinical or repair surgery for animal #A06010. The IACUC was provided with the list of surgeries already performed and with the veterinary examination results.

Motion: Dr. Phillips moved to approve the Significant Change request. Dr. Brabb seconded the motion.

Discussion Regarding the Motion: Dr. Hajjar commented that the surgical summary indicated abnormal behavior and that the animal was referred to the Psychological Well Being Program. Dr. Hajjar questioned as to whether or not the behavioral assessment had been completed prior to the last veterinary exam. Dr. Murnane confirmed that the animal's behavior is being monitored and further confirmed that the abnormalities noted would not affect the animal's suitability for the requested repair or clinical surgery. Dr. Cunningham suggested that a report regarding the behavioral abnormality be presented at the next IACUC meeting. Dr. Murnane agreed to bring the report to the next meeting for review. Dr. Batterson said that knowledge of the acronyms used in these reports would be helpful. Dr. Brabb commented that she thought they were standard acronyms and that it would be possible for the Committee to have a list. Dr. Murnane agreed to bring this list too.

Mr. Slosberg arrived.

Vote on the Motion: This motion passed unanimously with 12 members voting in favor.

❖ IACUC #2326-08 "Brain-Computer Interface for Primates" - Dr. Fetz

Dr. Phillips explained that the goal of the research is to develop treatments for spinal cord injury and stroke, using artificial circuits to connect brain signals to peripheral nerves and muscles. Dr. Phillips gave the Committee a moment to review the request and then summarized the three significant changes proposed for the Committee.

- **Brain stabilization:** The group requested to perform an additional step at the time of the initial craniotomy or in the second change (below) that would allow an alternative method for securing the pia to the dura and skull for stabilization during recording. Currently this is accomplished with a few drops of glue placed at the edge of the craniotomy. The new method would involve drilling several small holes anterior and lateral to the craniotomy for placing drops of glue or

silastic to bond the pia to the dura and skull. The modified technique would reduce movement-related shifts of the brain relative to the overlying skull and would help prevent loss of the neural signal recorded from the cortical electrodes that are attached to the skull.

- **Intracortical microelectrodes and subdural/epidural ECoG electrodes:** The request is for allowance to use different electrode arrays instead of the microwire electrodes that are currently approved. They would like to use one of three alternate arrays: 1) one intracortical and two subdural/epidural. In the latter case, they would perform either a subdural or an epidural array consisting of either 9-32 flat, gold electrodes (150µm diameter), or of up to 16 gold electrodes (300µm diameter).
- **Electrode positioning technique:** Currently positioning of microelectrodes during experimental sessions is accomplished by manually advancing the microelectrodes with the use of forceps. The requested change is for use of a small, light-weight microdrive to advance the electrodes in precise increments. The microdrive is 2-4cm in height and 2cm in width and would fit within the dimensions of the implanted cranial chamber. The microdrive would be positioned in the chamber by attaching it to the base using a miniscrew.

Motion: Dr. Phillips moved to approve the significant change request. Dr. Batterson seconded the motion.

Discussion Regarding the Motion: Dr. Cunningham asked if any of the surgeons had ever performed the tack down experimental procedure or is it a new idea that is being tested. Dr. Phillips replied that she did not know. Mr. McLean asked if the tack down procedure would change how the recording chamber was attached, and if so, would the procedure affect the frequency of how often the recording chamber would need to be replaced. Dr. Brabb replied that she did not believe that the change in procedure would affect the frequency of chamber replacement and Dr. Murnane concurred.

Vote on the Motion: This motion passed unanimously with 12 members voting in favor.

Approval of the Minutes

Dr. Cunningham called for the approval of the October 18, 2007 IACUC meeting minutes. Dr. Batterson moved to approve the minutes and Dr. Phillips seconded the motion. The minutes were approved with 10 members voting in favor and 2 abstentions.

Attending Veterinarian's Report

There was a sudden loss of heat in the K-wing on Saturday, 10/27/07. There were no animals harmed as a result of this event and all the investigators were notified. Specifically, temperatures dropped to 60 degrees F for several hours in a few rooms. This failure occurred again on Monday, 10/29/07, although temperatures didn't get as low. It was determined that the drop in temperature was due to a mechanical failure of a check-valve.

Protocol Monitoring:

♦ IACUC #3043-04 "Microdevices for Treatment of Presbycusis" – Dr. Ratner

Dr. Brabb reported that the animal work on this protocol has been stopped so the protocol has been removed from the veterinary monitoring program.

❖ **IACUC # "Mitogen Activated Protein Kinases: Role of Signal Transduction in Wound Healing and Infection" - Dr. Arbabi**

Dr. Brabb explained that the protocol studies potential therapeutic treatments for burn patients using a mouse model. The protocol had been placed on veterinary monitoring, and in October, the monitoring veterinarian reported that there were problems with research conduct. Drs. Cunningham, Brabb and Washington met with Dr. Arbabi and his technician. During the meeting it was determined that during one experiment in October 2007, only ½ the dose approved of buprenorphine was administered instead of the whole dose and supporting fluid had not been given consistently by the technician. Additionally, the pentobarbital dose listed in the protocol (40mg/kg) was not effective at getting the mice to a surgical plane of anesthesia, so the research staff had given 50mg/kg as a starting dose in the last experiment. Issues on recording of drug administration and organizing the experiments were also discussed.

As a result of the items noted above, Dr. Brabb monitored two experiments the week of 11/04/2007. In those experiments (6 mice each), 40 mg/kg pentobarbital did not provide sufficient anesthesia for any mouse and in all cases it had to be supplemented. Two mice did not recover from anesthesia in the first experiment. All mice recovered in the second experiment. After observing the experimental set up and the response to anesthesia, Dr. Brabb recommended that the group try isoflurane as well as list a wider dose range for pentobarbital in their protocol. Both significant changes have been turned in to the IACUC. Dr. Brabb provided the group with clarification regarding the record keeping necessary for each experiment and records were kept correctly for both of the experiments.

The above events were reported to OLAW.

Discussion: Dr. Cunningham asked if this was the groups first non-compliance. Dr. Brabb confirmed that it was. Dr. Cunningham asked the Committee was action they would like to take in response to the non-compliances. Mr. McLean suggested that a Letter of Counsel be sent to the PI. Dr. Brabb commented that given that the PI is a very busy Junior Faculty member and a surgeon, she thought it would be helpful to also send the Chair of the department a specific letter requesting that he/she provide the investigator with guidance as to appropriate research conduct. Dr. Phillips commented that she had some additional concerns. First, the Monitoring Veterinarian was not notified as to when the experiment was going to take place, and felt that this was a bigger issue than if a PI inadvertently leaves something out of their protocol and no animals are harmed as a result. Dr. Phillips further commented that during the initial review of the protocol, the IACUC felt so strongly that the animals would need to be monitored closely that the project was placed on Veterinary Monitoring as part of the approval. Dr. Phillips further commented that in spite of being on veterinary monitoring the monitoring veterinarian was not always notified in advance of the experiments; animals were burned and were not given fluids; and an analgesic dose was cut in half. As a result of the seriousness of the non-compliances, she felt that a letter of reprimand would be more appropriate, and should include language indicating that the Committee considers this to be a very serious situation, and if there is another non-compliance then the protocol could be suspended. Dr. Skerret asked why the group decided to reduce the analgesic dose. Dr. Brabb replied that because pentobarbital was a respiratory depressant, they decided to reduce the analgesic dose so that they would not compound the respiratory depression. Dr. Skerret said that respiratory depression would be less significant if they used isoflurane. Dr. Phillips commented that this is one of the issues that bothers her; the protocol was on veterinary monitoring so they should have consulted with the monitoring veterinarian for advice prior to making the change. Dr. Brabb commented that she will be observing the procedures where they are planning to use isoflurane. Dr. Pitts commented that he felt that the letter of reprimand should be copied to the Dean in addition to the Chair of the department.

Motion: Dr. Phillips moved to send the PI a letter of reprimand and include in the letter that if future non-compliances occur the project could be suspended. The department Chair and the School of Compliance should be sent a copy of the letter. Additionally, Dr. Phillips moved to send a letter to the departmental Chair recommending that they consider assigning a mentor to the PI to assist him in implementing his research program at the University. A response from the PI must include a plan to prevent this from happening in the future and assurance that the Monitoring Veterinarian will be notified of future procedures at least 48 hours in advance. Dr. Fitts seconded the motion.

Vote on the Motion: The motion passed unanimously with 12 members voting in favor.

❖ **IACUC #2331-01 "Bone Growth, Periosteal Migration, and Muscle Function" – Dr. Herring**

Dr. Brabb explained that the research uses pigs to study normal cranial function (food acquisition, chewing, swallowing) and how it affects skull biomechanics and growth. The study is relevant to clinical problems associated with abnormal biomechanics, such as facial deformities, muscle diseases, trauma repair, and predicting results of facial surgery.

In 2005, in conjunction with Veterinary Services, the group changed the analgesics given to pigs to include oxymorphone given pre-operately. The change provided smoother post-surgery recovery and was considered a refinement by Veterinary Services. When they restarted their second protocol in August of 2006, Veterinary Services did not realize that oxymorphone had not been added to this protocol as well. Therefore, in a total of 5 surgeries, oxymorphone was given to the animals even though it wasn't listed on the protocol. Dr. Brabb further reported that according to OLAW, this is a noncompliance as it is a change in analgesic and as such was reported to OLAW.

Discussion: Dr. Brabb stressed that the error was a Veterinary Services error. Dr. Phillips asked Dr. Brabb if she reported the non-compliance to OLAW as a programmatic non-compliance or as a protocol non-compliance. Dr. Phillips further commented that as she understands it, the PI contracts Veterinary Services to perform the procedures, so it's as if a Standard Operating Procedure (SOP) was not followed. Dr. Cunningham suggested that a letter should be sent to Veterinary Services regarding the error and a copy should be sent to the PI. Dr. Batterson suggested that Veterinary Services should re-review the SOP.

Motion: Dr. Batterson moved to send a Letter of Counsel to Veterinary Services reminding them that they need to read the protocol prior to initiating study procedures. Additionally, the letter should request that Veterinary Services notify the Committee as to how they will prevent this type of situation from occurring in the future. Dr. Fitts seconded the motion.

Discussion Regarding the Motion: Mr. McLean asked if any corrective action had taken place. Dr. Brabb confirmed that it had, and it was reported at the last IACUC meeting. Dr. Brabb further commented that this is an unfortunate situation, because Veterinary Services did the right thing clinically for the animal.

Vote on the Motion: The motion passed with 11 members voting in favor and 1 abstention.

Executive Secretary's Report

Report on packets sent:

Dr. Phillips reported that 2 packets were mailed since the meeting on October 18, 2007. The packets included 6 new protocols, 14 renewals, of which 9 were three-year renewals requiring a complete Project

Review Form. The other 5 renewals were annual renewals with morbidity or mortality reported. There were also 61 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.

Update on Communications Plan with Dr. Grue:

Dr. Phillips reported, that per the IACUC request, Dr. Grue submitted a communication plan for communications between his research group and Veterinary Services and the Office of Animal Welfare. Dr. Grue provided a contact list for Veterinary Services with contacts listed in order of preference for being contacted and specifically noted that he understands that if no one can be reached Veterinary Services will take any steps they deem necessary to protect the health and welfare of the animals. For the Office of Animal Welfare, he has provided contact information for himself and has requested that the Operations Manager continue to be copied on e-mails to him. Per the IACUC's request he has agreed that one of them will respond to communications within two business days. Dr. Phillips reported that the latter plan has been implemented fully and that her office is receiving responses as required.

Dr. Phillips reminded the Committee that Dr. Grue had requested that a revised letter be sent to him, and copied to those individuals who were copied on his previous letter, to clarify that there were no non-compliances with husbandry or with following veterinary orders. Once all clarifications were made, it was found that the real problem was in communications. The proposed letter would reflect this information. Dr. Phillips requested permission from the Committee to draft and send the letter, which would be signed by Dr. Cunningham.

Policy Review

- ❖ Anesthesia Policy – Dr. Phillips notified the Committee that the draft anesthesia policy that was voted on at the October 18, 2007 IACUC meeting had been rejected by OLAW. As is the current practice, all changes in anesthesia must be reviewed and approved by the IACUC.
- ❖ Guidelines for Non-Human Primate Neuroscience Studies - Dr. Brabb presented the two revised policies. The two draft revisions are essentially the same, however, the second draft revision would allow for 1 or 2 surgical sessions to be requested at one time. Dr. Brabb further explained that the reason why she drafted the second policy to allow for two surgeries is because when speaking with the Neuroscience PIs, they indicated that most of the animals have more than one implant, so more than one thing could require repair at any give time. Dr. Cunningham commented that the Committee does not know what the condition of the animal will be at the time that the second repair surgery is going to be performed. Dr. Brabb replied that prior to any surgery, the animals health is evaluated by the Primate Center veterinarians before the animal is cleared for surgery. This is why the IACUC exam was removed from the revised policy. Dr. Brabb further commented that the IACUC is charged with looking at the ethics of the situation and factor in the well-being of the animal rather than attempting to assess the clinical condition. Mr. Slosberg suggested that a possible solution might be to include a time-frame for which 2 surgeries is approved, and after the end of that period, the PI would need to come back to the Committee for approval to perform a second surgery. Dr. Vogel, a clinical veterinarian from the Primate Center was present at the time of the meeting and explained that in the past, the issue has been that a surgical repair is required, and then a few weeks later, something else breaks, requiring IACUC approval before the repair can take place. Dr. Batterson asked if there had been very many cases requiring the whole chamber to be replaced. Dr. Brabb replied that occasionally this happens and can think of one or two times where this has been an issue. The Committee asked for general clarification as to the revisions of the policies. For both policies the IACUC exam has been removed and all reference to clinical repairs has been removed. The first

policy only allows for approval of 1 surgery. The second policy allows for approval of 1 or 2 surgeries.

Motion: Dr. Brabb moved to approve the second policy as presented to the Committee. Dr. Hajar seconded the motion.

Discussion Regarding the Motion: Mr. Angelosante asked for clarification regarding surgeries and procedures conducted in one surgical session. Dr. Brabb confirmed that multiple procedures could be performed in one surgical session. Dr. Brabb agreed to revise the policy to indicate that two surgical sessions for "repair or repairs" can be requested. Dr. Fitts commented that one thing that requires attention when reviewing requests for multiple procedures are requested in one surgical session is the duration of the surgery. The Committee concurred.

Vote on the Motion: The motion passed with 7 members voting in favor and 5 members opposed.

The meeting was brought to a close at 4:02pm.

The floor was opened to public comment.