

Meeting Date: May 22, 2008

Members Present: J. Angelosante J. Cashman D. Fitts
 D. Lee N. Phillips S. Kelley
 I. Washington G. McLean T. Brabb
 P. Van Hooser (alternate for
 V. Batterson)

Members Absent: M. Slosberg W. Dickhoff R. Murnane
 S. Skerrett S. Cunningham

Opening Business:

Dr. Fitts called the meeting to order at 2:41pm.

Approval of the Minutes:

Dr. Fitts called for the approval of the April 17, 2008 IACUC meeting minutes. Dr. Brabb moved to approve the minutes and Ms. Cashman seconded the motion.

Discussion Regarding the Motion: It was noted that there was an error in the list of attendees at the April meeting. Ms. Petersen agreed to correct the minutes.

Vote on the Motion: The minutes were approved with 8 members voting in favor and 2 abstentions.

Attending Veterinarian's Report:

Reportable Event:

- 1) Cold water lines were contaminated with hot water in several rooms housing aquatic animals. The problem was detected by the alarms and the water was immediately shut off. However, the water temperature in one room reached 30° C. The following day, 5 zebrafish were found dead in that system, presumably from stress related to the elevated temperature. The plumbing issues were repaired by Facility Services. This incident was reported to the Office of Laboratory Animal Welfare.

- 2) On May 17, 18, 19, 2008 three rodent facilities at the University of Washington were out of the acceptable range of temperature (highest was 83 degrees). These high temperature events were caused by clogged lines carrying the cold water to the HVAC system (in two cases), and in one case, to a valve that had not been opened so cold water could reach that section of the HVAC system. In addition, there were temperatures out of range (too low) in one zebrafish room. No morbidity or mortality was associated with any of these events. A meeting is schedule with the individuals in charge of Facility Services to address these events. Dr. Brabb will let the IACUC know the outcome of this meeting.

Dr. Brabb reminded the IACUC that when they are conducting site visits they should emphasize to the personnel that all laboratory managers and/or responsible personnel must know how to contact Facility Services in the event of an HVAC issue.

Dr. Fitts asked if these incidents happened during the recent warm weather and Dr. Brabb said that it was.

Dr. Phillips notified the Committee that the OAW Decentralized Coordinator is working on a contact information sheet that will include Facility Services. It will be laminated and posted in the decentralized facilities.

Protocol monitoring:

Dr. Brabb reported that there was no activity on any of the protocols.

Executive Secretary's Report:

Report on packets sent:

Dr. Phillips reported that 5 packets and 1 emailed item were sent to the Committee since the meeting on March 20, 2008. This included the packet mailed on May 15, 2008 which was still under review at the time of the meeting. These packets and the e-mailed item included 13 new protocols. There were 43 renewals, of which 32 were three-year renewals requiring a complete Project Review Form. There were also 176 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.

Non-Compliance Report(s):

Dr. Phillips reminded the IACUC about a previously reported situation in which a technician used an incorrect euthanasia method during mouse colony maintenance procedures. Cervical dislocation was justified and approved on the IACUC protocol as a method of euthanasia for experimental mice but CO₂ should have been used for colony maintenance. The post-doctoral fellow did not understand that cervical dislocation should not be used to euthanize mice that were not being euthanized in order to collect data. The IACUC sent the fellow a letter of counsel requesting that he provide a description of procedures that he is allowed to perform and that he re-read the IACUC protocol and provide an assurance that he has done so. The letter to the PI requested that he review the protocol with the fellow to ensure clarity of approved procedures.

Both the fellow and the PI responded to the IACUC letters and provided the requested assurances. The PI had already discussed the situation with the fellow prior to receiving the letter. The PI was then out of town so another knowledgeable member of the group further reviewed the IACUC protocol with the fellow and gave him a refresher on overall animal use procedures. In addition, the PI met with both his chief animal technician and his laboratory manager to discuss the situation and there was also a laboratory meeting for the entire research group during which this issue was discussed and the importance of compliance was emphasized.

Anonymous Concerns:

- 1) Dr. Phillips reported that she received an anonymous letter of concern regarding an animal experiment. The letter indicated that a specific experiment was performed prior to approval of the Significant Change to the IACUC protocol. The letter further alleged that the experiment was

published. The publication and specific portion of the publication were noted. Dr. Phillips reported that she reviewed the publication and found the following information:

- As indicated by the complainant, the publication was first submitted to the journal prior to approval of the Significant Change to the IACUC protocol.
- However, the journal required revisions and the final version of the paper was not accepted until nearly 5 months after the Significant Change was approved.
- In addition, the publication is a collaborative effort as indicated by the fact that 3 of the authors, including the first author, are from foreign institutions. The publication states that all of the animal work was performed at one of the foreign institutions and that it was approved by their animal ethical board.
- The funding sources listed are not University of Washington sources.

Dr. Phillips indicated that she reported the letter to the Director of Compliance of the University's School of Medicine as required. The Director has had one meeting with the UW researcher and will meet with him again to further determine the UW's role in the publication, including whether any of the animal work was performed at the UW and if so, the timeframe in which the work was performed.

- 2) Dr. Brabb provided an update on the anonymous complaint that was filed several months ago related to the book chapter written by Drs. Laura Newell-Morris and Debra Durham; specifically, whether or not there was IACUC approval for the research published in the book. Dr. Brabb reported that she and Dr. Cunningham were not able to identify an animal use protocol that covered the pertinent period of time; however the retention period was reached so if there was an approved IACUC protocol it would have been shredded. Dr. Brabb reminded the Committee that there were other complaints in the letter that are not under the purview of the IACUC and they are being addressed by the Department of Anthropology and the School of Arts and Sciences.

Protocol Review:

- ❖ Kaneko, IACUC No. 2062-01 "Saccadic Eye Movement Studies" – Significant Change, Version 14, Animal No. A06010

Dr. Brabb summarized the animal's surgical history and explained that the PI was requesting approval for two repair surgeries.

Dr. Phillips asked what time-frame the surgeries were conducted? Dr. Brabb replied that the surgeries had been performed within the last year. Dr. Brabb further commented that the animal had been referred to the psychological well-being group. Dr. Kelley explained that the animal has been observed by that group but there had been no concerns for many months. Dr. Brabb summarized the psychological well-being report and noted that the animal remains on monitoring. Dr. Kelley explained that if at any time an animal has exhibited self injuries behavior, etc. then the animal would remain on monitoring until it is no longer at the UW.

Motion: Dr. Brabb moved that the Committee approve the Significant Change as written. Dr. Lee seconded the motion.

Discussion: Dr. Brabb explained that the PI is asking for two additional repairs for an animal that has had four repair surgeries in a short period of time. Dr. Brabb further expressed some concern about the number of repairs the animal has had and that she personally would not vote for two repairs at one time. Dr. Washington expressed agreement with Dr. Brabb's concerns. Mr. Van Hooser asked

whether the request specifically identified the type of repair. Dr. Brabb explained that it was a general request for two future repairs because they do not know what might fail.

Dr. Fitts asked if the animal would still be useful if one repair was performed and then there was a delay while a second repair was requested and approved. Dr. Brabb explained that this would not be an issue. Dr. Brabb further explained that if the animal required a clinical surgery there would be no need for IACUC approval prior to performance of the clinical surgery.

Vote on the Motion: – The Significant Change was unanimously disapproved with 10 members voting in opposition.

2nd Motion: Dr. Brabb moved to approve one additional repair surgery for A06010. Dr. Washington seconded the motion.

Discussion: None.

Vote on the 2nd Motion: The motion passed unanimously with 10 members voting in favor.

❖ Kaneko, IACUC No. 2062-01 “Saccadic Eye Movement Studies” – Significant Change, Version 15, Animal No. Z05353

Dr. Brabb summarized the animal’s surgical history and explained that PI was requesting approval for one repair surgery.

Motion: Dr. Brabb moved to approve the Significant Change Request. Dr. Washington seconded the motion.

Discussion: None

Vote on the Motion: The motion passed unanimously with 10 members voting in favor.

❖ Phillips, IACUC No. 4146-01 “Electrical Stimulation of the Vestibular Nerve” – Significant Change Version 16, Animal No. A06011

Dr. Brabb summarized the surgical history and explained that Significant Change request was for one additional repair or revision surgery.

Motion: Dr. Brabb moved to approve the Significant Change Request. Dr. Washington seconded the motion.

Discussion Regarding the Motion: Dr. Fitts asked if the repair would cover all surgically implanted equipment. Dr. Brabb replied that it would. Dr. Phillips went over the surgical summary again, noting the duration of time between surgeries. Ms. Cashman asked for clarification of the Significant Change request and Dr. Fitts re-summarized the request for the Committee. Mr. Van Hooser asked what was involved in a vestibular implant repair or revision. Dr. Brabb explained that it involves a slight repositioning of the originally implanted electrodes or the receiver stimulator.

Vote on the Motion: The Motion passed with 9 members voting in favor and 1 member opposed.

❖ Phillips, IACUC No. 4146-01 “Electrical Stimulation of the Vestibular Nerve” – Significant Change Version 1, Animal No. A05033

Dr. Brabb summarized the surgical history and explained that the Significant Change request was for one additional repair or revision surgery.

Motion: Dr. Brabb moved to approve one additional repair for animal A06011. Dr. Kelley seconded the motion.

Discussion Regarding the Motion: Mr. Van Hooser asked Dr. Brabb about the combination of eye coil repairs/replacement and recording chamber repair/replacement into one repair event. Dr. Brabb explained that the eye coil and recording chamber are connected so if they are replacing a chamber they need to replace the leads to the eye coil.

Vote on the Motion: The motion passed unanimously with 10 members voting in favor.

❖ Fetz, IACUC No. 2326-08 “Brain Computer Interface for Primates” – Significant Change Version 33, Animal No. L04057

Dr. Brabb summarized the Significant Change request for the Committee. Dr. Brabb explained that a repair to remove the cylindrical casing and implant a new micro-wire array, then re-affix the casing to the original position was requested and approved for this animal at the March 20, 2008 IACUC meeting. The repair was initiated but the implantation of the micro-wire array was never performed because the chamber was too difficult to remove.

For the previous Significant Change request Dr. Fetz provided an explanation as to why the animal is uniquely valuable to the study. Because the explanation was relevant for this request Dr. Brabb read Dr. Fetz’s explanation as follows:

“Animal L04057 is uniquely valuable insofar as it will self-administer electrical stimulation to the subcortical site. The process of finding a reinforcing site was laborious and time-consuming, lasting for more than one year (June 2006 to June 2007). Finding such a site was a prerequisite to the final phase of the experiment described in protocol 2326-08: ‘operantly conditioning changes in neural activity via electrical stimulation of a positive reinforcing site, through continuous operation of a brain-computer interface (Neurochip) during free behavior’. We recently confirmed the feasibility of this protocol in this monkey, by successfully conditioning electromyographic activity during free behavior. Obtaining stable cortical neural signals is now essential for the final phase of the experiment. The placement of another micro-wire array in a fresh region of the cortex is essential for obtaining results from this study.”

Dr. Brabb summarized the animal’s surgical history and explained that the Significant Change request was for a repair surgery to implant guide tubes over the right hemisphere, where the dura is unscarred and relatively soft and remote from other implants. They would keep the rods inside the guide tubes to prevent their blockage and they would orient the guide tubes so that they are perpendicular to the dural surface. The approximate angle for each implant site would be calculated using their magnetic resonance image of the animal’s head.

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

Discussion Regarding the Motion: Dr. Brabb summarized the animal's surgical history. Dr. Phillips summarized the outcome of the previous electrode implant surgeries so that the Committee would have a better understanding for this request. Dr. Fitts asked if they were getting any useful data from the current electrodes. Dr. Brabb replied that they were not. Dr. Brabb told the Committee that in her personal opinion she felt they should be allowed to try this one more time because the animal has had a lot of procedures performed already and she would hate for it to amount to nothing as that would be a waste of the animal. Dr. Phillips asked if the procedure works this time, what will be the process after that for data collection, etc. Dr. Brabb commented that she also had concerns for the continuation of the experiment if this procedure is successful. Preston asked how many guide tubes would be inserted and Dr. Brabb did not know. Preston asked if the PI was planning to have the non-functioning guide tubes removed and filled. Dr. Brabb did not know. Dr. Kelley commented that he was concerned that the animal has had quite a few procedures and complications as a result of these procedures and without better understanding of why an additional animal could not be used he would have a hard time approving the request. Discussion followed regarding the Committee members questions about the procedures, animal history, and necessity to continue the study and use of this animal. Because there were so many questions that could not be addressed, Dr. Phillips suggested that the PI be contacted to see if he could come to the meeting in order to address the Committee's questions. Dr. Perlmutter, who is the Co-PI on the project was contacted and agreed to come to the meeting immediately.

The meeting was temporarily adjourned at 3:40pm to allow for the arrival of Dr. Perlmutter and staff.

Dr. Fitts called the meeting back to order at 3:50pm.

Drs. Perlmutter and Eaton arrived to answer the Committee's questions. Dr. Brabb asked how many guide tubes would be implanted. Dr. Perlmutter replied that 4 tubes would be implanted. Dr. Brabb asked Dr. Perlmutter what the time-frame for the procedure would be. Dr. Perlmutter said that in the past when they have conditioned muscle activity it has taken less than a week. Dr. Brabb asked if after that the recordings would be taken and then the experiment would be over. Dr. Perlmutter said that after completion of the recordings he was not sure if it would be the end of the animal's experimental procedures on the study, but that it would be the end of that experiment. Dr. Brabb asked why the animal had EMG electrodes and if they were functional. Dr. Perlmutter explained that they wanted to see if they could condition a physiological signal in the cage with their brain computer interface. Muscle activity is a lot easier for them to record, so they wanted use this operant conditioning paradigm using this easier signal. Dr. Perlmutter further explained that their main intent is to condition neural activity and that requires the guide tube implantation procedures. The muscular conditioning portion of the experiment is complete.

Dr. Fitts asked for an explanation of the scientific rationale for continuing with this animal rather than using a new animal. Dr. Eaton explained that the animal is fully trained and already has the reward site, which is a site where a stimulating electrode had been implanted, and the animal will work for the stimulations. He further explained that this was the biggest obstacle in their training.

Dr. Fitts asked the PI to reiterate the timing for the animal if the Significant Change was approved and the procedure completed. The PI explained that once they are done collecting data the animal will be immediately euthanized but they want to use the animal for as long as the recordings are stable using the existing implants. Dr. Phillips asked for assurance that if they could get even a weeks worth of data that this information would still be valuable, and would allow them to finish the experiment that they are in the middle of. Dr. Brabb asked whether they have to do the EMG muscle stimulation paradigm in the same animal in which they do the neuronal stimulation paradigm. Dr. Eaton said that it is not a requirement but it saves the cost and time of re-implantation.

Vote on the Motion: The motion passed with 7 members voting in favor, 2 members opposed and 1 abstention.

The meeting was brought to a close at 4:04pm.

The floor was opened to public comment.