

Meeting Date: August 21, 2008

Members Present:	W. Dickhoff	J. Cashman	C. Hotchkiss
	D. Lee	N. Phillips	V. Batterson
	I. Washington	M. Slosberg	J. Angelosante
	S. Cunningham	R. Murnane	T. Brabb
	D. Fitts		

Members Absent:	S. Skerrett	G. McLean	T. Reh
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**Opening Business:**

Dr. Cunningham called the meeting to order at 2:34pm.

**Approval of the Minutes:**

Dr. Cunningham called for the approval of the July 24, 2008 IACUC meeting minutes. Dr. Dickhoff moved to approve the minutes and Dr. Batterson seconded the motion.

Discussion Regarding the Motion: Dr. Washington noted that the animal number A95088 was incorrectly listed as A98088 and the minutes should be revised to include the correct animal number.

Vote on the Motion: The minutes were approved with 11 members voting in favor and 1 abstention.

**Attending Veterinarian's Report:**

Protocol Monitoring:

Dr. Brabb reported that there are two protocols on protocol monitoring and there has been no activity on either protocol since the last IACUC meeting.

Adverse Event:

Dr. Brabb reported on an event that occurred on a research protocol that involves a microbial evaluation preclinical trial where blood samples are collected at time points following intravaginal installation of microbial gel and subsequent intravaginal installation of SHIV. On July 29, 2008 twenty animals were involved in a portion of this study. Because of the time points required, the final sedation and blood collection occurred at approximately 6pm. One animal, a 17 year old female macaque, was found dead the next morning. Gross necropsy did not reveal any significant lesions. Histopathology is pending. The primate center veterinary staff interviewed the two staff members who conducted the study and determined that this animal may not have fully recovered from the ketamine anesthesia. The death could be associated with anesthetic complications. The staff stated that not all animals were maintaining a sitting posture when last observed.

Re-training of the staff involved occurred immediately. They were reminded that purposeful movement was not an adequate indication of recovery from anesthesia; adequate recovery in macaques is defined as the ability to achieve and maintain an unsupported sitting posture without stimulation. They were also reminded that older, somewhat obese animals may not metabolize sedating agents as effectively as

younger, better conditioned animals. Therefore, the low end of the dose range needs to be used in older animals. Dr. Brabb further noted that this event was reported to OLAW.

Discussion: Dr. Brabb suggested that the protocol PI and the WaNPRC Associate Director each be sent a letter asking them to provide the Committee with corrective measures that will be taken to prevent this type of incident from recurring in the future. Drs. Brabb and Hotchkiss also discussed the possibility of revising the Event Recording form suggesting the addition of criteria such as "sitting up" on the form as a step after "return to cage".

Dr. Brabb further explained to the Committee that the research staff members were on site at the time of the incident, but there was a miscommunication between them and the animal was not re-checked.

Revised Motion: Dr. Brabb moved that a letter be sent to the protocol PI and the WaNPRC Associate Director asking how they are going to prevent this type of event from occurring in the future. Dr. Hotchkiss was asked look into whether a post-procedure form modification is practical and to report back at the next IACUC meeting. Dr. Fitts seconded the motion.

Discussion: Dr. Fitts asked if the animal's death would have been preventable if the animal had been re-checked. Dr. Brabb explained that histopathology will probably not reveal a definitive cause of death, but she thought if it was a ketamine reaction there would have been a good chance that treatment could have prevented its death. Dr. Hotchkiss concurred, but it was re-iterated that they do not know if this would have been possible and they may not be able to determine whether or not treatment would have been successful.

Vote on the Motion: The motion passed with 11 members voting in favor and one abstention due to conflict of interest.

Mr. Slosberg arrived at 2:46 after completion of the vote for the items noted above.

### **Executive Secretary's Report:**

#### **Report on packets sent:**

Dr. Phillips reported that 2 packets were sent to the Committee since the meeting on July 24, 2008. These packets included 5 new protocols. There were 31 renewals, of which 19 were three-year renewals requiring a complete Project Review Form. There were also 62 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.

#### **Overview of IACUC site visits since spring 2006:**

Dr. Phillips provided the IACUC members with a chart illustrating the findings from semi-annual site visits dating from spring of 2006. She noted that the number of deficiencies sited has changed over time and that some of the increases for certain categories are probably a result of more training and greater scrutiny by site visitors after the summer 2006 AAALAC visit. Dr. Phillips commented that for example, in 2008 there was an increase in deficiencies in the sanitation category.

Drs. Batterson and Brabb commented that items such as cloth chairs and mops left on the floor fell into this category. Dr. Batterson further commented that in the Spring of 2008 a lot of groups were changing labs which likely contributed to deficiencies such as holes in the wall, etc. Mr. Slosberg suggested that

common findings could be reported back to the PIs so that they would pay more attention to preventing the commonly identified deficiencies.

Dr. Cunningham suggested that an email summarizing, for example, the top three deficiencies or areas that deficiencies were noted for the last site visit period could be sent out to the PIs every 6 months. The Committee agreed that this sounded like a good idea and a plan for disseminating the information should be developed. Dr. Cunningham commented that she thought the Committee should review the summary of deficiencies every 6 months.

Dr. Phillips thanked Ms. Taylor and Ms. de Hoyos for their efforts in preparing the summaries.

#### **Protocol Review:**

- ❖ Phillips, IACUC No. 4146-01 "Electrical Stimulation of the Vestibular Nerve", version 18  
Dr. Washington summarized the surgical history for animal Z05357 and explained that the Significant Change request was for the approval of two repair surgeries. Dr. Washington commented that some of the surgical scenarios noted are actually clinical surgeries so do not require IACUC approval.

Motion: Dr. Washington moved to approve one additional repair. Dr. Brabb seconded the motion.

Discussion: Mr. Slosberg asked why Dr. Washington suggested approval of only one repair. Dr. Washington explained that she personally felt that only one repair should be approved at a time. Dr. Fitts commented that most of the surgical repairs summarized in the request were clinical surgeries. Dr. Phillips commented that the group already needs to use one of the requested repairs. Dr. Fitts asked if failure of the vestibular implant was common. The Committee reviewed several other animals' clinical records but could not determine an answer to the question. Dr. Brabb reiterated that the group plans to perform a surgery and will not have a repair available if only one surgery is approved. Dr. Washington commented that she would want to know if another vestibular implant was necessary shortly after the scheduled repair. Dr. Cunningham suggested that the Committee ask the PI to explain what is happening with the vestibular implants. Dr. Fitts asked if the nature of the failures is known. Dr. Brabb suggested that Dr. Washington modify her motion to approve one repair and to request an explanation for the equipment failure. Dr. Murnane suggested that they also ask how many animals are having these issues.

Revised Motion: Dr. Washington moved to approve one repair and a letter should be sent to the research group asking for an explanation as to why the implants are failing and how many animals are affected.

Vote on the Motion: The motion passed unanimously with 13 members voting in favor.

- ❖ Phillips, IACUC No. 4146-01 "Electrical Stimulation of the Vestibular Nerve", version 19

Dr. Washington summarized the surgical history for animal Z05355 and explained that the Significant Change request was for the approval of two repair surgeries. Dr. Batterson said that she does not understand what "revision" means. Dr. Brabb explained that revision means that the original implant is moved slightly to access another area of the brain for recording.

Motion: Dr. Washington moved to notify the PI that they have a repair available so their Significant Change request for a repair would not be approved. Dr. Batterson seconded the motion.

Discussion: Dr. Phillips explained that she did not think that a repair was available. The Committee re-reviewed the surgical history and determined that the PI does need approval for repair surgery.

Revised Motion: Dr. Washington moved to approve one repair and ask for clarification of what a revision entails. Dr. Batterson seconded the motion.

Discussion: Dr. Murnane said that he wants to know how often revisions are happening. Dr. Phillips suggested that the issue regarding the revisions could be addressed in a letter separate from the approval letter. Ms. Cashman asked if the Committee should consider not approving the surgical request until after the response is received from the PI. Dr. Cunningham replied that if the Committee waited for a response the PI would not be able to perform a repair for at least another month. The Committee felt that it was not necessary to hold approval of the repair until the response was received. Dr. Brabb suggested that the length of time that the implant needs to stay in place also be asked. Dr. Washington suggested that the letter being sent to the PI should request clarification of the terms "revision" and "repair". The Committee agreed to send a separate letter addressing the general questions regarding the repairs.

Vote on the Motion: The motion passed unanimously with 13 members voting in favor.

❖ Phillips, IACUC No. 4146-01 "Electrical Stimulation of the Vestibular Nerve", version 20

Dr. Washington summarized the surgical history for animal A08001 and explained that the Significant Change request was for the approval of two repair surgeries.

Motion: Dr. Washington moved to approve one surgical repair or revision. Dr. Batterson seconded the motion.

Discussion: Dr. Brabb commented that it seems that the loss of three out of three head lugs is not typical. Dr. Cunningham suggested that this could also be addressed in the letter to the PI.

Vote on the Motion: The motion passed unanimously with 13 members voting in favor.

❖ Letter to Dr. Phillips Regarding Vestibular Implants, Repairs and Revisions

Motion: Dr. Washington moved to send a letter to Dr. Phillips requesting the information noted below. Dr. Fitts seconded the motion.

- 1) Why are the vestibular implants failing?
- 2) What is a revision vs. a repair?
- 3) How often are the head lugs failing and why?
- 4) How long do the vestibular implants need to stay in place?
- 5) What is the frequency of equipment failure in all animals on study?

Discussion: None

Vote: The motion passed unanimously with 13 members voting in favor.

## Protocol Review Continued

### ❖ Anderson, J., IACUC No. 3382-04 "Vitality of Trinidadian Guppies"

Dr. Dickhoff summarized the protocol explaining that the goal of the study is to examine and improve a vitality model and to explore two mechanisms of lethal stress: energy loss and oxidative stress. There are two main studies as part of the protocol, as follow.

The Growth and Heterogeneity Study aims to examine the survival capacity among individuals at various levels of heterogeneity produced by varying growth rates.

The Transformation of Vitality Distribution Study aims to compare different measures of energy and oxidation to survival capacity (vitality parameters).

Additionally, they will conduct a pilot study using 151 guppies to determine surrogate endpoints to replace spontaneous mortality. As part of the pilot there are three measures that could relate to the quality of the fish to time mortality will be tested. 1) time to loss of equilibrium when exposed to an anesthetic dose of MS222, 2) time to reach a spotlight, and 3) spontaneous loss of equilibrium. Guppies will be introduced to challenge of increased water temperature and starvation but prior to spontaneous mortality for most guppies, these surrogate endpoints will be tested.

Dr. Dickhoff explained that the group purchases the guppies from pet stores or obtains them from other research groups. Dr. Dickhoff recommended that they get them from other PIs if possible, in order to ensure the health of the fish.

Dr. Dickhoff summarized the Committees questions based on the review of the protocol as part of the August 7, 2008 Copy to Committee.

Motion: Dr. Dickhoff moved for approval of the protocol pending the PIs response to the committee's previous questions. Dr. Batterson seconded motion.

Discussion: Dr. Brabb asked about the temperature of the water for the increased temperature challenge. Mr. Slosberg replied that they will be acclimated to 23°C and then the water temperature will be raised to 32°C. Dr. Dickhoff confirmed that this was correct.

Dr. Batterson asked why it was necessary to use 151 fish in the pilot study. Dr. Dickhoff explained that the PI had not done this study in guppies before so he based the number on a salmon study. Dr. Batterson asked if there was any possibility they would not need to use so many animals. Dr. Dickhoff replied that they may end up using less fish because they have used salmon in previous studies so there may be a smaller variation using guppies thus less animals will be required. Dr. Batterson asked if it was necessary to use 151 fish to determine how many fish will die. Mr. Slosberg replied that they are trying to determine the variability in the signs of morbidity. Dr. Phillips explained that in the main study they would like to be able to euthanize the fish. In the pilot study they are trying to determine a surrogate endpoint for death, but they don't know if there are going to be signs that are definitive of imminent death. Dr. Dickhoff said that there are other parameters that they will use such as body weight to determine whether or not the animal will die.

Dr. Batterson commented that it seems that if they can't find surrogate endpoints then the entire project would be death as an endpoint. Dr. Hotchkiss agreed. Dr. Cunningham suggested that the

Committee could approve the pilot project and then ask the PI to report the results to the Committee for review prior to voting on the main study. Mr. Slosberg said that the protocol is very clear that they will conduct a pilot study to determine surrogate endpoints.

Dr. Cunningham asked about the practicality of using the attraction to light study as a surrogate endpoint given the time that it would take to conduct the study on each fish. Dr. Dickhoff said he is not sure about the timing of the study but it may be possible with multiple testing tanks and the use of video tape. Dr. Brabb commented that the problem with not approving the entire study is that the group is setting up a breeding colony. Dr. Phillips commented that the PI has submitted a study to use death as an endpoint, but because he does not want to use death as an endpoint he proposed a pilot study to try and determine surrogate endpoints to death. Dr. Phillips further commented that in most cases a PI will submit a study with death as an endpoint and the Committee will require them to do a pilot study to determine that there are no alternatives. Dr. Washington said that it seemed to her that the PI had already given up on the possibility of finding a surrogate endpoint. Dr. Phillips replied that based on her conversations with the PI she does not believe that this is the case. Dr. Cunningham asked if the Committee could just approve the pilot project and then review the data prior to approving the main project. In the mean time, he could just breed fewer fish. Dr. Batterson commented that the issue for the Committee to consider is if the Committee would vote not to approve the main project if it is determined that death as the endpoint is necessary. Dr. Brabb commented that she felt the Committee should vote on the project as submitted.

Dr. Fitts commented that regarding the species justification, the protocol said that guppies are the ideal system for the research, but later in the protocol it said that they are using guppies because the PI has no experience with zebrafish. Dr. Dickhoff confirmed that the group has more familiarity with guppies, but he does not know if either guppies or zebrafish would necessarily be a better model and guppies adapt well to captivity. Dr. Fitts commented that if the group was concerned about getting healthy guppies, then maybe they would want to use another species. Dr. Dickhoff said that there are healthy guppies available.

Dr. Fitts asked about the potential issues associated with anesthetizing the fish three times per day. Dr. Brabb agreed that this was not clear, and suggested that the Committee ask the PI to provide clarification as to the number of times the fish will be anesthetized per day as well as potential complications as a result of frequent anesthesia.

Revised Motion: Dr. Dickhoff moved that the Significant Change request be turned over to the Designated Reviewer method and that he be appointed the Designated Reviewer. Dr. Batterson would be appointed the secondary reviewer and Dr. Fitts would serve as the back up reviewer.

Vote on the Motion: The motion passed with 12 members voting in favor and one member voting against the motion.

❖ Fuchs, A., IACUC No. 2342-01 "Oculomotor System Studies", version 27

Dr. Washington summarized the surgical history for animal A08003 and explained that the Significant Change request was for the approval of an eye coil replacement and a chamber replacement in the event that either is necessary.

Motion: Dr. Washington moved to approve one surgical session during which an eye coil or head chamber could be repaired or replaced. Dr. Batterson seconded the motion.

Discussion: Dr. Batterson commented that it seems like they are having problems with the eye coil. Drs. Phillips and Brabb replied that there is not enough history with this eye coil to be able to tell if there might be chronic issues. Dr. Batterson said that she misunderstood and thought that an eye coil repair was necessary right now. Dr. Brabb clarified that the group is asking for a future repair surgery.

Vote on the Motion: The motion passed unanimously with 13 members voting in favor.

❖ Feigl, E., IACUC No. 2036-07 "Coronary Physiology" version 24

Dr. Brabb summarized the study and explained that the Significant Change request is to change the pre-anesthetic/analgesic drug used in their acute anesthetized dog preparation. The group is currently using morphine but because morphine is causing histamine release in some of the dogs resulting in high heart rates and low arterial pressures, the PI would like to use oxymorphone.

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

Discussion: None

Vote on the Motion: The motion passed with 12 members voting in favor and one abstention due to conflict of interest.

**Other Business:**

Dr. Cunningham introduced Dr. Hotchkiss, explaining that she is replacing Dr. Kelley on the Committee since he retired.

**Closing Business:**

The meeting was brought to a close at 3:48pm.

The floor was opened to public comment.