

University of Washington
November 17, 2016 IACUC Meeting Minutes

Members Present:

AS	JS	NK
CG (Public)	JPI	PB
CH	KL	SH
JB	MG	SL
JM	ML	TB
JPVH	MT	

Members Absent: AB CG (Scientist)

Opening Business:

The IACUC Chair called the meeting to order at 2:31PM

Approval of the IACUC Meeting Minutes

The IACUC Chair called for the approval of the October 20, 2016 IACUC meeting minutes.

Motion: A motion to approve the minutes as written was made and seconded.

Discussion: None

Vote on the Motion: The meeting minutes were approved with 11 members voting in favor and 4 abstentions. KL and MT were not present for the vote.

Benefit Story – JS

This month's benefit story [Ramos & Chamberlain 'Gene Therapy for Duchenne muscular dystrophy' *Expert Opinion Orphan Drugs* 3:1255-1266 (2015)] comes from the Chamberlain lab, whose research aims to find a cure for Duchenne muscular dystrophy, a relatively common inherited disorder that causes severe progressive muscle weakness starting around the age of four, and typically leads to death from cardiac or pulmonary failure within just 10 to 20 years. The cause of this muscle weakening is the loss of a protein called dystrophin, and the Chamberlain lab has been developing a gene therapy treatment that can replace the defective dystrophin gene with a healthy copy. Working with rodent and canine animal models of Duchenne muscular dystrophy, the Chamberlain lab has found that viral vectors can be used to direct the expression of healthy dystrophin in muscle cells that lack dystrophin and restore relatively normal muscle function and extend life span. The development of this gene replacement therapy holds tremendous promise for curing Duchenne muscular dystrophy by permanently addressing the root cause of the disease.

Attending Veterinarian's Report:

Facility issues:

Humidity: No recent reports of low humidity

Temperature and lights:

We have one centralized facility that is having swings in temperature greater than four degrees multiple times during the day (not every day, but often. Greatest

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swings seen are 6 degrees F). DCM has been working with facility services to clearly identify the problem. From the newest data, it appears that when the temperature begins to rise in the room, the HVAC systems overshoots when it corrects the temperature. We are going to ask physical plant to propose a solution and then decisions will need to be made by central administration as to whether those solutions are cost-prohibitive. In that case, the facility would need to be closed. I will provide an update monthly until it is resolved.

Protocol Monitoring:

There are 15 active protocols on the veterinary monitoring program. Nine involve surgery, anesthesia and surgery, or restraint and surgery. Five involve other procedures including one that involves tumor monitoring.

Adverse events:

Three incidences in the last two months of water-related mortality I need to discuss and one incidence of mice found without food in their hopper. All of these incidences have occurred at separate facilities. In all instances, the animal technicians and researchers have been retrained. Emails have been sent out to remind people of the proper procedures.

1. One mouse was found dead in its cage on 10/4/16 with a water bottle flipped upside-down. The cage had been changed the day before.
2. A cage containing 4 male and 2 female mice was found with the water bottle flipped up on 10/1/16 (animals in the cage had been weaned on 9/26/16). There was an empty gel container in the cage. One male was found dead, two mice did not respond to treatment and were subsequently euthanized and the remaining mice recovered.
3. 1 of 3 mice were reported dead on 10/28/16. The cage was marked with a red dot and did not have a Lixit valve. The cage was setup by the researcher on 10/26, he saw the red dot, but did not remember the significance of it.
4. Two cages of mice (5 total) were weaned on 10/31/16 and then found dead on 11/7/16 in a cage with no food in the hopper.

In addition to retraining, DCM is investigating the possibility of an equipment change in the water bottle facilities that would put a "post" in the back of the cages without lixits that would make them stick out if they were put on a rack that had a lixit.

In addition, TB will be meeting with the animal technicians to discuss this issue with them, and see if they have additional ideas of methods to improve detection of these issues early. We have in the last 6 months been urging animal technicians not to pull out the cages during health checks unless they really need to, as we were seeing increased cannibalism in breeder cages that may have been associated with pulling out of the cages. The cannibalism issue has resolved.

Discussion: The Committee wanted to know whether or not any of the involved PIs had prior issues, however, it was not known for certain whether or not the PIs were at fault. TB stressed that the key to addressing this issue is to make people aware and to provide training. SH wanted to know what constituted training and TB explained the training emphasis.

HBA Subcommittee:

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The HBA committee met this month and the veterinary staff presented information regarding clinical cases of disease in nonhuman primates and pigs, as well as up-dates on some projects involving large animals, but the majority of time was spent discussing the non-compliance that we will be discussing later.

OAW Director's Report – summary in folder

STI reminded the IACUC that the Deficiencies at a Glance (DAAG) are in folder and asked that people get corrections or comments back to us as we are compiling the deficiencies for the semiannual report which will be reviewed by the IACUC in January.

SOPs/Policies/Guidelines

- Blood Withdrawal Policy
TB summarized the changes to the policy. TB asked everyone to run through the examples and make sure that they can follow them.

Discussion: The Committee had some suggestions for clarifying the exceptions section. AS had grammar suggestions. The Committee discussed the application of the policy. It was suggested that the IACUC provide a template for calculating the blood draws and TB and STI agreed to explore this possibility.

Motion: A motion was made and seconded to approve the policy with the suggested changes. TB moved to approve with changes.

Vote on the Motion: The motion passed unanimously with 17 members voting in favor.

- Primate procedures, suggested wording and guidelines for protocols – TB asked that the IACUC take some time to look it over and bring suggestions back to the Committee at the next meeting.

Adverse Events:

- 4154-01 - STI explained that there was an incident involving one mouse on this study. As part of the approved monitoring plan, if weight loss reaches 20% or greater of starting body weight Veterinary Services is to be contacted and if weight loss exceeds 30% for two consecutive days, the animal will be euthanized. In this case, the student on the protocol used the weight from the previous day rather than the pre-study weight and incorrectly calculated the weight loss. The mouse had exceeded the weight loss limit and subsequently died.

Motion: A motion was made and seconded to send the PI a letter of counsel to remind the him that all animal work must be done in accordance with his approved IACUC protocol and that he is responsible for ensuring that his staff is properly trained and IACUC-approved procedures are followed. The Committee recommended that as a tool to help prevent this mistake in the future, the group calculate the weight that would be too low (less than 80% of pre-study weight) and put that weight on the weight log for reference.

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The Committee requested that he reply to this letter indicating the steps he will take to prevent future occurrences of this nature.

Discussion: The Committee discussed how this happened and made suggestions for indicating the weights outside of the approved weight loss.

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

- 4314-08: STI explained that the issue involved blood overdraws in NHPs, which were first reported as an anonymous concern. STI explained that the PI was present and asked her to provide some background. NK summarized the purpose and importance of the protocol.

The Committee reviewed 4 items and the circumstances surrounding these items and the corrective action that was taken in order to determine whether or not there was a non-compliance or an area of concern for each. 1) blood overdraws 2) discrepancies between the 'example' timeline and wording in Section II.11., 3) blood draws and sedation events in an animal that had been identified as anemic, and 4) requests for samples from individuals who were not listed as personnel on the protocol. The following motions were made to determine whether or not each were a non-compliance.

The Committee thoroughly reviewed the circumstances surrounding these issues and the corrective action that was taken.

1. Blood Draw Volumes

Motion: A motion was made and seconded to consider the blood overdraw a non-compliance.

Vote on the Motion: The motion passed with 13 members voting in favor and 1 member opposed.

2. Discrepancies between the 'example' timeline and wording in Section II.11.

Motion: A motion was made and seconded to consider the 'example' timeline and wording an area of concern.

Vote on the Motion: The motion passed with 8 members voting in favor and 6 member opposed.

3. Blood draws and sedation events in an animal that had been identified as anemic.

Motion: A motion was made and seconded to consider the care of the anemic animal an area of concern.

Vote on the Motion: The motion passed with 13 members voting in favor and 1

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member opposed.

4. Requests for samples from individuals who were not listed as personnel on the protocol.

Motion: A motion was made and seconded to consider the personnel not on the protocol an area of concern.

Vote on the Motion: The motion passed with 13 members voting in favor and 1 member opposed.

Based on the decisions made above, the IACUC suggested that a Letter of Counsel be sent to the PI and Associate Director of the WaNPRC.

Motion: A motion was made and seconded to send the PI and the Associate Director of the WaNPRC Letters of Counsel, summarizing the Committee's decisions.

The letter to the PI should stress the gravity of the errors and to emphasize that it is ultimately the PI's responsibility to ensure compliance with her protocol, regardless of external time-lines and pressures, noting that her acknowledgement of her responsibility was not apparent to the committee when she spoke to the IACUC at the meeting. The Committee requested that she reply to the letter confirming receipt, acknowledging the gravity of the situation and accepting responsibility for all activities that occur on her protocol. Additionally, the IACUC asked that she provide them with assurance that adequate mechanisms have been put in place to ensure that this does not happen again.

The letter to the Associate Director of the WaNPRC should also stress the gravity of the errors, and to emphasize his responsibility for ensuring compliance, regardless of external time-lines and pressures. Additionally, the Committee wanted to impress upon him the importance of veterinary oversight, so appropriate safeguards are in place to ensure the health and wellbeing of the animals. The Committee requests that he reply to the letter confirming receipt, acknowledge the gravity of the situation, and provide assurance that adequate mechanisms have been put in place to ensure that this does not happen again.

Discussion: Individuals involved with the protocol left the meeting. IACUC members, TB, NK and CH also left the meeting due to conflict of interest. The Committee had a detailed discussion of the issues, the circumstances surrounding the issues and the corrective action that was taken.

Vote on the Motion: The motion passed with 13 members voting in favor and 1 member opposed.

With regard to the impact of this non-compliance on the reporting of data from this NIH-funded study, the Committee understands that the PI is working with STI to determine which data points will be unpublishable.

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HoverBoard – EW provided the IACUC with a project status update.

Closing Business:

The Meeting was brought to a close at 4:33 pm. The floor was opened to public comment.