

University of Washington
December 17, 2015 IACUC Meeting Minutes

Members Present:

AB	MG	JM (Scientist)
JB	CH	MN
PB	ML	JS
TB	SL	JPVH
EC		

Members Absent:

MB	CJ	JM (Member)
CG (Scientist)	NK	MT
CG (Public)		

Opening Business

The IACUC Chair called the meeting to order at 2:36pm.

Protocol Review:

- Dr. Ramsay, 2452-05, V.32 “Behavioral Pharmacology of Nitrous Oxide”

JPVH introduced the PI and explained that the Significant Change was being reviewed at the meeting because additional pilot data was requested in support of a grant application due in early March 2016.

Two modifications have been proposed in rats.

One pilot study measures drinking saccharine-sweetened water. This did not generate any questions or concerns during the pre-review by several IACUC members and vets. Two rats were requested for this pilot.

The other modification involved a study that would test whether there is an association between an individual’s heat production response during a nitrous oxide administration and the heat production response made by that same animal when it is given a brief cold challenge. Recent results from the PI’s lab published in PlosOne (2015) indicate that a rat’s heat production response during an initial nitrous oxide administration predicts that individual rat’s degree of subsequent drug consumption. The PI wants to increase the translational value of this work by determining whether a non-drug cold challenge can substitute for a drug exposure in predicting an individual’s vulnerability to developing addiction like behavior. The NIH grant reviewers were excited about this study but wanted to see pilot data suggesting that this relationship might exist. Twenty rats requested for this pilot.

In essence, Dr. Ramsay has proposed to give rats a brief cold exposure and a brief nitrous oxide exposure 1-week apart (in counterbalanced order) while measuring each rat’s heat production response to see if a rat’s response to these two different types of challenges are correlated with each other.

The PI was available to answer questions raised by the Committee but as there were none, left the meeting.

Motion: A motion to approve the Significant Change was made and seconded.

Discussion: None

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Vote on the Motion: The Significant Change was approved unanimously with 13 members voting in favor.

- Dr. Waldorf, 4165-01 V. 58 Experimental Model for Chorioamnionitis and Preterm Labor

CH summarized the Significant Change. The protocol is currently approved to perform an experiment to infuse 500 micrograms of lipopolysaccharide (LPS) into the amniotic fluid of their nonhuman primate model. Their goal was to induce preterm labor, which did not occur in the first 2 days. The protocol is currently approved to inoculate LPS a second time if the first dose does not induce preterm labor within 3 days. They would like approval to increase the dosing range of LPS from a maximum of 500 micrograms to 5 milligrams per inoculation to improve our chances of inducing preterm labor. The new dose range on the protocol would be 10 micrograms – 5 milligrams of LPS.

ML asked when the second dose of LPS would be administered. The PI replied that they want to induce labor as soon as they can and intended to give the second dose at 3 days. ML suggested that the PI include a range of 3-7 days in the protocol. The PI agreed.

The Committee discussed the frequency of monitoring of the animals after injection. It was explained that researchers monitor the animals for 6 hours after injection visually and by monitoring data remotely including temperature and uterine contractions. The Committee felt that the animals should be monitored at least every 15 minutes in the first hour.

Motion: A motion was made and seconded to approve the Significant Change with the addition a range of 3-7 days for administration of the second dose and to also include that the animals will be monitored every 15 minutes for the first hour after administration of the second dose.

Discussion: None

Vote on the Motion: The Significant Change was approved unanimously with 13 members voting in favor.

IACUC Training: Preparation and Use of MS222 – ML

- MS-222 is a powder that is used as both an anesthetic and a euthanasia agent in fish, and the powder is used to prepare a water bath. According to the safety data sheet for MS-222, it may cause mild skin and eye irritation, and “dust may be irritating to the mucous membranes and upper respiratory tract. May be harmful if inhaled.” EH&S is currently updating the recommendations for MS-222 that are attached to protocols, so that they are more explicit that MS-222 powder must be measured in a fume hood (i.e., you can prepare a concentrated liquid stock solution in the hood that you can then work with outside of the hood). On our site visits, when site visitors visit labs that work with aquatic animals and use MS-222, they should remember to ask where the powder is weighed. The Committee discussed the following:
 - 1) Solutions should be labeled with the date the solution was made, the concentration and the expiration (“use by”) date.
 - 2) Researchers will be required to bring their balance into the fume hood for preparation of MS222.

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- 3) Changes to the policy were made because the previous policy did not require preparation in the fume hood as long as it did not generate aerosol. As a result of the AAALAC site visit the policy was revised to require preparation in a hood. The EH&S policy is also being updated to reflect this change. There is still discussion regarding preparation of this agent while in the field.

- **Use and Storage of f/air Canisters - TB**

Site visitors should check to make sure researchers are weighing the canisters. Canisters should be disposed of when there is an increase of 50 grams in weight. It was explained that after use, they must be bagged or stored in a fume hood because anesthesia will leak out over time. They should not be placed in the trash. JB commented that EH&S is working on outreach to let people know how to properly store and dispose of the canister. This topic was included in the EH&S newsletter that just went out today.

- **Training Updates - EC**

As part of our ongoing training for IACUC Site Visitors, a new training module was developed which focuses on review of protocols and associated documents, many of which are encountered during site visits. The Mock protocol will be available to the IACUC training site. Members were asked to complete training by January 11, 2016.

Approval of the IACUC Meeting Minutes

The IACUC Chair called for the approval of the November 19, 2015 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 12 members voting in favor and 1 abstention.

The Benefits of Research – JS

The IACUC Chair introduced a new agenda item, which would be used to alert the IACUC to the advancements made by UW researchers as part of their IACUC protocols. The journal article noted was ‘Targeted, activity-dependent spinal stimulation produces long-lasting motor recovery in chronic cervical spinal cord injury.’ McPherson JG, Miller RR, Perlmutter SI. Proc Natl Acad Sci U S A. (2015) 112:12193-8. PMID: 26371306

Attending Veterinarian’s Report

Facility issues:

- **Humidity:**

Low humidity was reported in a centralized facility caring for NHPs and one case of bloody nose was noted, that was severe due to a clotting deficiency. This facility should have working humidity control. Central Administration and Facility Services are aware of the problem and Facility Services is working on a permanent solution. The Committee would be updated on the solution in January.

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- **Temperature and lights:**

On November 17, 2015 lights remained on outside of the normal light cycle in one centralized rodent room after an error in programming. The light control was modified when animals were moved out so that facility repairs could be done. However, the over-ride was not removed when the animals were moved back. This was discovered during the routine process that is in place to check the light cycles in all rooms and was fixed the next day. The animals had one night in which the lights did not turn off.

Protocol Monitoring: There are 14 protocols on the veterinary monitoring program. Ten protocols involve surgery, 2 involve restraint and surgery, 1 involves anesthesia and other procedures, and 1 involves other procedures. One protocol, 4261-01 will be removed from protocol monitoring. This protocol was added in May 2015 after Veterinary Services noted some post-surgical infections. The group has been retrained, and the infection issues have been resolved.

Adverse Events:

- Protocol 4282-01: This investigative group studies interventional treatments for prostate cancer. They received 15 approximately 3-month-old LPB-Tag transgenic mice from another institution on October 1, 2015. According to their approved protocol, the mice would be used immediately in a study to monitor the bio-distribution of magnetic nanoparticles. However, they were not used immediately, as there was some variation in age and some of the mice had not developed tumors yet. On November 29, 2015 two mice were reported to veterinary services and found to be lethargic and dehydrated with distended abdomens. They were euthanized, and gross necropsy revealed markedly enlarged prostate tumors exceeding the tumor size limit in the protocol. Veterinary Services met with the group and will facilitate them putting in a significant change with more appropriate timelines and monitoring parameters for this strain of mice. In addition, they have been added to the veterinary monitoring program. This will be reported to OLAW.

Motion: A motion was made and seconded to send a Letter of Counsel to the PI to remind him that all animal work must be done in accordance with the approved IACUC protocol. The Committee requested that the PI reply to this letter indicating the steps that will be taken to ensure that members of the lab are aware of approved procedures as well as how he will prevent future occurrences of this nature.

Discussion: The Committee discussed the timeline for the animals from arrival at the UW to euthanasia.

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

- Protocol 4361-01: This groups studies new interventions in the diagnosis and treatment of renal failure. As part of a significant change, they added streptozotocin-induced diabetes in a mouse model to their protocol in order to induce diabetic nephropathy. The individual running the study and the PI consulted with other investigative groups regarding additional monitoring parameters after the study began as they became worried the mice would decline secondary to the development of diabetes. As part of these different parameters, they increased the frequency of blood sampling, outside what was in the protocol, and started administering insulin to some mice (3). No mice were harmed, the amount of blood taken was minimal, however none of these changes were included in the protocol. Veterinary Services met with the group and discussed significant change mechanisms and what constitutes a significant change. Veterinary Services was working with the group to develop a

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significant change to add some of the increased monitoring and the potential for insulin administration. This will be reported to OLAW.

Motion: A motion was made and seconded to send the PI a letter of counsel to remind him that all animal work must be done in accordance with the approved IACUC protocol. The Committee requested that the PI reply to the letter indicating the steps will be taken to ensure that members of his lab are aware of approved procedures as well as how he will prevent future occurrences of this nature.

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

Harm Benefit Analysis (HBA) Subcommittee:

TB updated the IACUC on the activities of the HBA subcommittee. They had discussed the food and water restriction policy that would be presented to the IACUC today, had reviewed one protocol for categorization of pain and distress and had discussed issues of morbidity and mortality seen by the veterinary staff in the last month.

OAW Director's Report – Summary slide in folder

AAALAC Site Visit – The visit went well. There were some suggestions for improvement (SFI) that led to some slight modifications in some policies and practices. The plans for site visit training discussed at today's meeting will touch on the key items identified.

Protocol Non-Compliance

Protocol 4154-01: During a site visit last summer it was noted that there were several days where the temperature in the room varied and should have been reported to Veterinary Services and Facility Services for correction. Additionally, during the site visit a cage of mice was found on a table, with no cage card. Veterinary Services was contacted to follow up on these mice.

The lab-managed space has been closed and the group will be moving to centralized housing.

MN asked STI to describe the condition of the mice. STI said that the mice appeared hunched and there was a noise coming from cage but she was not sure of the origin of the noise. It was clarified that the procedures performed on the mice were approved by the IACUC. A Significant Change to address the monitoring has been submitted to the IACUC.

Motion: A motion was made and seconded to send the PI a Letter of Counsel to remind him that all animal work must be done in accordance with the approved IACUC protocol and that he is responsible for conduct of his staff and ensuring that IACUC approved procedures are followed. The technician involved will be copied on the letter but was not required to respond. The Committee requested that the PI reply to the letter indicating the steps will be taken to ensure that members of his lab are aware of approved procedures as well as how he will prevent future occurrences of this nature.

Discussion: The Committee discussed the circumstances surrounding the mice. The main concern was ensuring that the animals are monitored appropriately post-procedure because they are housed for 3 days on a heating pad and could over heat if there was a malfunction.

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

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Centralization Subcommittee

A Subcommittee will be established to review exceptions to the standard of centralized technician monitoring. The Husbandry Special Service Request form would be used for researchers to make their case for monitoring to be provided by members of their group. The Subcommittee would be appointed by the IACUC Chair and would consist of JS, DCM staff, IACUC members and other appropriate experts. These requests will be put in a subcommittee folder for evaluation. SL volunteered to be on the Committee.

IACUC SOPs and Policies:

- **Dietary and Fluid Restriction in Mice, Rats – TB**

The Committee reviewed the policy and it was determined that the word fluid should be changed to water.

Discussion: It was mentioned that the policy did not include the step of assigning a pain or distress category in the same way that the Non-Rodent USDA Species policy does. The Committee could ask the Harm Benefit Committee to review these for pain/distress classification and this could be added to the policy. The Committee did not pursue this change.

Motion: A motion was made and seconded to approve the policy with the proposed change of wording from ‘fluid’ to ‘water’.

Vote on the Motion: The policy was approved unanimously with 13 members voting in favor.

- **Dietary and Fluid Restriction in Non-Rodent USDA Species – TB**

The Committee was asked to review the policy prior to the January meeting where it would be presented for a vote. It was determined that the word ‘fluid’ should be changed to ‘water’.

- **Non-pharmaceutical Grade Substances in Laboratory Animals – ML**

This is a new policy. In recent years there has been an increased regulatory focus on limiting the use of non-pharmaceutical grade compounds in research animals. The Committee has been asking more questions about non-pharmaceutical grade compounds in protocol review; however, it is clear that a policy is needed to help formalize the expectations for both the IACUC reviewers and the research groups. The Committee discussed the inclusion of additional compounding pharmacies and the addition of a clarifying statement regarding the fact that oral drugs should only be given orally. Additionally, a recommendation of the pharmacy standard regarding expiration dates would be added.

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

Vote on the Motion: The policy was approved unanimously with 12 members voting in favor. JM was not present for the vote.

- **Analgesia in Research Animals policy – ML**

The proposed additions (yellow highlight) were made to address the fact that some form of analgesia should be “on board” when animals recover from anesthesia following painful procedures such as surgery. This is something veterinary staff have been trying to address in protocol review; however, there are certain cases where the chosen combination of anesthetics and analgesics does not safely allow for immediate post-op analgesia.

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One example is the use of ketamine/xylazine anesthesia in rodents with an opioid such as buprenorphine for analgesia. In this case, veterinary services does not recommend that buprenorphine be given until the animals are beginning to recover from K/X anesthesia, in order to avoid excessive respiratory depression. However, unless another analgesic is added, such as local anesthetics used at the incision line or pre-or peri-operative administration of an NSAID, the animal may have a period of inadequate analgesia during the immediate post-op period depending on the severity of the surgery.

The purpose of editing this policy is to formalize and explain the expectation that multimodal analgesia may be necessary in some cases in order to safely provide immediate post-op analgesia.

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

Vote on the Motion: The policy was approved unanimously with 12 members voting in favor. JM was not present for the vote.

- **Veterinary Verification and Consultation and Timing of Procedures, Timing of Administration of Agents, and Changes in Procedures - TB**
TB explained that changes were made to the policy to include behavioral testing. The Committee discussed this option and the types of procedures and circumstances that would apply. The Committee determined that they were not comfortable with the changes to the policy at this time and the revision was not put to a vote.

Closing Business:

The Meeting was brought to a close at 4:46pm. The floor was opened to public comment.