

University of Washington
February 16, 2017 IACUC Meeting Minutes

Members Present:	AB	JM	MG
	AS	JPVH	PB
	CG (Scientist)	JS	SH
	CG (Public)	JPI	SL
	CH	KL	TB
	JB	*NG	

Members Absent: NK

*NG Alternate for ML

Opening Business

The IACUC Chair called the meeting to order at 2:32 pm.

Approval of the IACUC Meeting Minutes

The IACUC Chair called for the approval of the January 19, 2017 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 2 abstentions.

The Benefits of Research – JS

Worldwide, more than 1 million sexually transmitted infections are acquired every day with potentially devastating consequences for reproductive health. ‘The mucosal surfaces of the genital tract are the site of entry to over 30 different bacterial, parasitic, and viral pathogens that are the cause of sexually transmitted infections... including HIV’¹. New preventative vaccines and treatment options are needed to manage the global health burden of sexually transmitted infections, but the complex environment of the mucosal immune system presents unique challenges to vaccine and drug development.

The Woodrow lab in the Bioengineering Department here at UW has been studying the anatomy and mucosal immune system of the female reproductive tract using non-human primates to better understand the microflora, hormones and specialized immune cells that influence this biological environment and its response to sexually transmitted pathogens¹. These studies are critical for the design of effective vaccines against sexually transmitted diseases.

The Woodrow group has also been using mice to develop nanolipogels, which are biocompatible compounds that can be used to deliver anti-HIV drugs directly to the vaginal mucosa, serving to protect against infection².

These innovative studies that combine basic biology and advanced material engineering hold tremendous promise for the development of novel treatments of one of the major health issues of our time.

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¹Ramanathan and Woodrow 'Engineering immunity in the mucosal niche against sexually transmitted infections' *Wiley Interdiscip Rev Nanomed Nanobiotechnol* 8: 107-122 (2016)

²Ramanathan, Jiang, Read, Golan-Paz and Woodrow 'Biophysical characterization of small molecule antiviral-loaded nanolipogels for HIV-1 chemoprophylaxis and topical mucosal application' *Acta Biomater* 36: 122-131 (2016).

OAW Director's Report

Total CTC Reviews 2/16/2017											
	1/18/2017 via email	1/19/2017 CTC	1/24/2017 via email	1/26/2017 via email	1/26/2017 CTC	1/31/2017 via email	2/2/2017 CTC	2/3/2017 via email	2/9/2017 CTC	2/13/2017 via email	Total
New Projects	0	1	0	0	1	0	1	2	4	0	9
3-Yr Renewals	0	1	0	3	0	2	1	0	0	0	7
Annual Rnwls	0	2	0	0	2	1	16	0	5	0	26
Sig Change	1	6	1	0	7	0	10	0	14	1	40
VVCs	0	0	0	0	0	0	1	0	0	0	1
Admin Change	0	0	0	0	0	0	0	0	0	0	0
Standard Substances and Procedures	0	1	0	0	0	0	0	0	0	0	1
Total Items	1	11	1	3	10	3	29	2	23	1	84

Site visit reports - DAAG

Read responses to NHP incidents – dehydration and cage change – response letters were read to the committee.

Primate center representatives were asked to address questions.

Personnel continued animal care under supervision.

Cage change – AT supervisor gave the AT permission to delay cage change

AT supervisor responsible for oversight of AT even after the mortality of the NHP.

Discussed staffing, animal condition, record accuracy, technological fix?,

Read letter from OLAW regarding 0796 001 – discussed what the implications are.

Update Regarding the Completion of Instillation of Safety latches in cage washer “On January 26, 2017, the production company, Omega Medical Mechtronics made the lever assemblies and welded them into the door jam”

Attending Veterinarian's Report

Facility issues:

Humidity: Low humidity in many facilities and there has been reports of nose bleeds in one NHP. All animals have responded to treatment or resolved on their own.

Temperature and lights: No reports

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Protocol Monitoring:

There are 14 active protocols on the veterinary monitoring program. At this time they are all going well. One of the reviews we have today is one of the protocols on monitoring.

Adverse event:

On December 12, 2016 a *Macaca nemestrina* on protocol “Experimental Model for Viral Induced Brain Injury”, # 4165-02, died while under anesthesia. This project is studying Zika virus and the animal involved was pregnant with a due date of 1/11/17. She was inoculated with Zika virus on 9/21/16, and underwent periodic blood collection and MRI as part of the experimental protocol. No clinical abnormalities had been noted on routine observations or physical examination.

On 12/12/16 she was given ketamine and propofol as pre-anesthetics, and anesthetized with sevoflurane for experimental MRI. Once in a stable plane of anesthesia, she was transported to the MRI which involves putting the animal in a special transport container. When they arrived at the MRI, the technician found that the MRI had been cancelled. They were at the MRI for approximately 15 minutes, during which the animal was closely monitored the entire time. After various phone calls confirmed that the MRI would not be done, the animal was again closed in the transport container, and made the 5 minute walk back to the primate center surgery suites. When the veterinary technician opened the transport container in the surgery suite, the animals color was grey and it had stopped breathing. She phoned the veterinarian on call, who was there within a minute, but resuscitation efforts were not successful.

A full necropsy was performed. Histologic findings include minimal myocardial fibrosis with chronic epicarditis, and mild cerebral congestion and chronic perivascular hemorrhage. The pathologist suggests that the cause of death is likely to be an anesthesia reaction.

This type of anesthetic death would normally be reported to you, but typically I would not be asking for any additional action. However, when the supervisor veterinarian reviewed the anesthetic records, she found that anesthetic records for trips to the MRI in the last year, were incomplete. Initial drugs were recorded as needed, but then the full record (which usually takes recordings of vital signs approximately every 10 minutes) were not started until the animal was already in the MRI (no records after induction and before transport or immediately on arrival). I would not expect records to be completed in the hall, but I would expect readings prior to leaving the surgery suite, and then immediately upon arrival at the MRI. This appears to be a drift in procedure, not something only done by one individual.

The purpose of charting the vital signs (writing down a series of numbers, generally graphically) in a case is to give the anesthetist a visual, long term view of the case, so that subtle, slow changes are detected, which generally take hours or at least 30 minutes to develop. Sudden changes are pretty readily observed by watching the animal. Charting anesthetic cases isn't just a regulatory action that is done at UW, but is considered standard of care by veterinarians throughout the country. I recommend following the guidelines from the American Association of Veterinary Anesthesiologists regarding frequency and types of recordings. This means vital signs are recorded typically every 10 minutes. Of course, if you are busy with the patient, a particular time point may be missed or extended as the most important part of being an anesthetist is to observe the patient, and monitor the patient, not just the numbers. So, if you view a record and a time point is missed, that alone is not an issue, so please understand the difference if you are out on a site visit and looking at anesthetic records. But repeatedly missing chunks of time is not appropriate.

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The supervisory veterinarian has made changes in the procedure and retrained all the staff to chart these anesthetic events appropriately. In addition, she has assigned two people to each procedure, rather than just one, in order to help provide adequate manpower to do the charting and still properly monitor the anesthesia, especially around the times of transport and repositioning in the MRI. I talked to the veterinary technician involved, and I believe her understanding of anesthesia is what I would expect from someone with her training, and I also believe she was monitoring the animal appropriately as she could respond to specific questions.

The lack of record keeping for anesthetic trips to the MRI is out of line with appropriate care, and thus, in my opinion, is a noncompliance. How the drift in procedures happened is unclear, but it appears to be related to staffing changes. The direct supervisor in this case discovered the issue and brought it directly to my attention.

However, I would recommend that we send the primate center a letter of reprimand for this issue as providing adequate staff and staff training is vital to animal care, and there have been several different issues suggesting to me that re-evaluation of staffing and how training is performed may be needed.

Motion: by (TB) It was motioned that we send a letter of reprimand to the director of WaNPRC citing this incident and the previous incidents where there has been drift (blood draw volumes and cage changes) – examine staffing, training and general oversight issues. {seconded by SL} Would like the Director to come back and inform the IACUC of their plan. Discussion ensued.

It was decided that a subcommittee would prepare the letter – TB, PB, JI, SH, CH, STI.

17 in favor; no opposed. Motion passed.

HBA Subcommittee:

The HBA committee met this month. The topic of discussion was clinical and experimental issues of morbidity or mortality. I would like to thank everyone for his or her attendance.

For those of you who have not attended an HBA subcommittee meeting, I would encourage you to attend at least once a quarter (3-4 times a year). We can hook up video or audio remote feeds.

Protocol Review

Dr. Robinson, 4310-01, V.127 “Role of Cerebellar Nuclei in Eye Movement Control and Adaptation”

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

Discussion: The Committee discussed the animal's implant history. Noted that the protocol specified that they use males and this animal is a female. No scientific reason to use males only; results are scientifically valid in both males and females.

Vote on the Motion: The Significant Change was approved unanimously with 16 members voting in favor. 1 abstention (because the member left the room for the discussion).

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Kiem – Surgery Classification of Laparoscopic Mesenteric Lymph Node And Spleen Biopsy

Laparoscopic surgery on Kiem protocols

Purpose of IACUC discussion: To characterize a new laparoscopic surgery in non-human primates as major or minor. This survival surgery has been or is being added to protocols 3235-03 and 3235-04. The IACUC has a responsibility to determine whether this is a major or minor surgery.

Relevant excerpts from Page 117 of The Guide:

“Laparoscopic surgeries... may be classified as major or minor surgery depending on the impact on the animal (Devitt et al. 2005; Hancock et al. 2005; NRC 2003; Perret-Gentil et al. 1999, 2000). For example, laparoscopic techniques with minimal associated trauma and sequelae (e.g. avian sexing and oocyte collection) could be considered minor, whereas others (e.g. hepatic lobectomy and cholecystectomy) should be considered major... Whether a laparoscopic procedure is deemed major or minor should be evaluated on a case-by-case basis by the veterinarian and IACUC.”

“As a general guideline, major survival surgery (e.g. laparotomy, thoracotomy, joint replacement, and limb amputation) penetrates and exposes a body cavity, produces substantial impairment of physical or physiologic functions, or involves extensive tissue dissection or transection (Brown et al. 1993). Minor survival surgery does not expose a body cavity and causes little or no physical impairment; this category includes wound suturing, peripheral vessel cannulation, percutaneous biopsy, routine agricultural animal procedures such as castration, and most procedures routinely done on an “outpatient” basis in veterinary clinical practice. Animals recovering from these minor procedures typically do not show significant signs of post-operative pain, have minimal complications, and return to normal function in a relatively short time. When attempting to categorize a particular surgical procedure, the following should be considered: the potential for pain and other postoperative complications; the nature of the procedure as well as the size and location of the incision(s); the duration of the procedure; and the species, health status, and age of the animal.”

This group’s research focuses on the study of the HIV reservoir in nonhuman primates and the development of novel cell and gene therapy strategies to target and eradicate the viral reservoir, and repopulate the hematopoietic system with HIV-resistant cells.

A “Laparoscopic mesenteric lymph node and spleen biopsy” survival surgery was recently added to one group on protocol 3235-03, and there is an amendment for 3235-04 that will be in this week’s committee packet that adds this surgery to all groups on that protocol. The surgery consists of creating up to three 3-6mm incisions into the abdomen, one for the camera and two instrument ports. Up to 3 mesenteric lymph nodes are collected, and up to 3 pinch biopsies are collected from the spleen. Hemorrhage is controlled with cautery, and fibrin glue or a gelatin sponge may be used to control bleeding from the spleen biopsy sites. The incision sites are closed with suture. The procedure is reported in the protocols to take 30-40 minutes per animal, and no post-surgical deficits are not anticipated. The animal will receive at least 48 hours of peri- and post-operative analgesia. Other procedures may be performed at the same time points, such as upper and lower GI biopsy, peripheral lymph node biopsy, CSF collection, bone marrow aspiration, and/or bronchoalveolar lavage. These are all minor surgeries non-surgical procedures.

For reference, in December 2014 the IACUC evaluated a request adding laparoscopic mesenteric lymph node biopsies only. In that instance the IACUC voted that the surgery was minor. In October 2015 the IACUC evaluated a laparoscopic mesenteric lymph node and liver biopsy surgery in conjunction with rectal, colon, and jejunal biopsies, and voted to classify those together as major.

Motion: TB moved that this be classified as major, seconded by CG.

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Discussion: Asked about whether the liver and spleen biopsy would be different. Discussion about the repetition of the procedure (frequency and repeated surgeries of the same type). Every time you do a procedure, there is the potential for herniation at the incision site. Relatively long procedure (30-40 minutes). Given the full event of all the procedures also increases the classification as major vs minor.

Vote on the Motion: 15 in favor, 2 abstentions.

(JM left the room)

SOPs/Policies/Guidelines

- B.1110 Environmental Enrichment for Sheep - TB

Motion: TB moved to approve SOP as written, SL seconded

Discussion: Asked about mirrors and types of music.

Vote on the Motion: 16 approved; no abstentions.

- NHP EE SOP - CH

Motion: CH moved to approve SOP as written, SH seconded

Discussion: Asked if there were any issues – responded that there were no issues.

Vote on the Motion: 16 approved; no abstentions.

Closing Business:

The Meeting was brought to a close at 4:44 pm. The floor was opened to public comment.