

UNIVERSITY OF WASHINGTON OFFICE OF ANIMAL WELFARE

September 1, 2020

TO: National Institutes of Health (NIH)

SUBJECT: Notice of Institutional Animal Care and Use Committee Approval

(eGC1 A146864)

The following application has been reviewed and the associated IACUC protocols are approved. The grant/contract and the associated IACUC protocol are concordant in terms of animal use.

Principal Investigator: Zijun Liu

Grant Title: The Tongue Base in Respiration and Swallowing

IACUC Protocol Number: 3393-05

Protocol approval dates: 9/1/20 - 8/31/23

The project as proposed meets the standards of the Guide for the Care and Use of Laboratory Animals and applicable University policies and procedures. The University of Washington has an approved Animal Welfare Assurance (#A3464-01) on file with the NIH Office of Laboratory Animal Welfare (OLAW), and the University is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International.

Michelle Brot, Ph.D.

Review Scientist, Institutional Animal Care and Use Committee

Office of Animal Welfare

Michelle Brot

University of Washington, Box 357160

Seattle, WA 98195-7160

Phone: 206-221-0891, Fax: 206-616-5664

From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Thursday, November 5, 2020 3:58 PM

To: Bob Ennes; Michelle Brot

Subject: FW: Liu Pig Swallowing Protocol

HI Bob,

These are the only communications I had with Michelle re: this protocol.

Does my name/institution get redacted? I'm not an employee of the UW.

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA

Director | Animal Resources
Attending Veterinarian
Benaroya Research Institute at Virginia Mason
1201 Ninth Avenue | Seattle, WA 98101
p 206.342.6967
BenaroyaResearch.org

From: Andrew Burich

Sent: Monday, August 31, 2020 10:27 AM **To:** Michelle Brot <mbrot@uw.edu> **Subject:** RE: Liu Pig Swallowing Protocol

HI Michelle,

I need to pass this back to you to work with Zee on getting this protocol in shape. I am spending way too much time with this and I have other amendments in my inbox to review.

Briefly,

he added a special diet procedure for high fat chow for the pigs based on one of my questions....then he removed it. However, if you look in Aim 2 Husbandry Exceptions – when talking about barium he mentions a high fat diet. So not sure if the pigs are or aren't being fed a high fat diet.

Also, for some reason, he changed his "Other: Liu-Minipig: Terminal recording (Team)" into "Behavioral Testing (with Food or Fluid Restriction): Liu-Minipig: Terminal recording, ver. 1 (Team)".

I'd be grateful if you could help with this.

Thanks,

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA

Director, Animal Resources
Benaroya Research Institute at Virginia Mason
1201 Ninth Avenue | Seattle, WA 98101
p 206.342.6967
BenaroyaResearch.org

From: Michelle Brot <<u>mbrot@uw.edu</u>> Sent: Monday, August 24, 2020 4:13 PM

To: Andrew Burich aburich@benaroyaresearch.org; Molly K. Lucas mklucas@uw.edu>

Subject: Re: Liu Pig Swallowing Protocol

Hi Andrew,

Thanks for your thorough review of this and your eagle eyes! I think Molly and I both had reviewer fatigue by the time we were done so clearly we missed editing the surgery procedures. The explanation is that Molly suggested that since Vet Services retains discretion on how they want to proceed with the pig anesthesia, it would be best (and consistent with other large animal procedures) to have an attached list of every possible anesthetic agent that might be used and have the procedure refer to that. That change was made for at experiment level but hadn't been caught within the surgery procedures. I will go ahead and make the swap so that the <u>Substance Administration: Liu-Minipig:</u> <u>Anesthesia Protocol (Team)</u> procedure replaces the Vet Services Administered Anesthetics procedure.

Feel free to get in touch if you find any more inconsistencies (I promise, we didn't hide them for you intentionally!! ©

~Michelle

From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Monday, August 24, 2020 3:19 PM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Liu Pig Swallowing Protocol

Hey there,

Before I ask the PI this question, I thought maybe you could help me out.

This is for Aim 1, but may apply to Aim 2: I noticed that in **Survival Surgery: Liu-Minipig: Implantation (Team)** he lists on pg2, Q4 a procedure for Vet Services Administered Anesthetics. However, this is completely different than **Substance Administration: Liu-Minipig: Anesthesia Protocol (Team)** that is in the Procedure List.

Which is correct? The one in the survival surgery procedure needs to be edited because it talks about sleep devices.

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA

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Benaroya Research Institute at Virginia Mason
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p 206.342.6967

BenaroyaResearch.org

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From: Molly K. Lucas <mklucas@uw.edu>
Sent: Sunday, August 23, 2020 10:07 AM

To: Kim Stocking

Subject: Fw: Zee Liu pig protocol

fyi - not sure if this has been discussed yet.

Molly

From: Molly K. Lucas

Sent: Sunday, August 16, 2020 1:35 PM **To:** Michelle Brot <mbr/>brot@uw.edu> **Subject:** Zee Liu pig protocol

Hi Michelle,

I just turned around my 2nd vet consult. One thing I didn't put in Hoverboard but wanted to ask you to think about, is that in response to my recommendation to add some flexibility in timing in Q #5 of the experiments, he added, "Please note that the following timelines are approximate, and subject to be modified upon the detailed situation." I think this is an improvement, because sometimes things happen like the MRI isn't available, or a fasting mistake is made, and procedures have to be put off a day or two. I am thinking that there are often more specific parameters around this, though, esp in large animal protocols (e.g., I've seen some that say the timeline could vary but "up to x days").

Might be a good topic to check in with the other reviewers on to see what they think/how they've been approaching this type of thing.

Thanks, Molly From: Molly K. Lucas <mklucas@uw.edu>
Sent: Monday, July 27, 2020 4:33 PM

To: Michelle Brot

Subject: Fw: Zee pig protocol

fyi

Molly

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 4:28 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu> Subject: Re: Zee pig protocol

Hi Nick,

That sounds great to me - I'd much rather not try to review it until you've had a chance to work through the anesthesia plan and those changes are incorporated. I agree that plan seems much more efficient. I'll enter a comment to meet with VS and make any edits and resubmit, that way it's not sitting in vet consult and the message is clear that the meeting is the first step of the vet consult process.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu>
Sent: Monday, July 27, 2020 4:21 PM
To: Molly K. Lucas <mklucas@uw.edu>
Cc: Kim Stocking <kstock@uw.edu>

Subject: Re: Zee pig protocol

Hey Molly,

Zi actually reached out to VSreview on the 21st for a review of the anesthesia for this project. I had Alex email back to set up a meeting for us to all get together and come up with an anesthesia plan (me, Gary and the anesthesia resident). I think that tends to work much better with him than trying to dig into his descriptions and go back and forth. I'd like to try to get a chance to meet with him before going too critically into his descriptions because I think the plan is likely to change after we meet. Unfortunately, he has not responded to our email. I am asking Alex to reach out again and include me so that I can urge him to meet with us soon if possible. Do you think this is doable or should we just review as is written.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu
206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 3:49 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu>

Subject: Zee pig protocol

Hi Nick,

Zee's pig protocol is in vet consult now. Michelle wrote the following - apparently there is some grant-related time sensitivity:

Zi-Liu has received a grant and has resurrected his minipig protocol. Please prioritize this as the funding agency is waiting for its approval. Nick is very familiar with Zee's procedures and also, Zee e-mailed Gary Fye and asked him to review the Anesthesia procedure description to make sure it sounds consistent with what Vet Services does.

Maybe we can both go through it and compare notes?

Thanks, Molly From: Molly K. Lucas <mklucas@uw.edu>
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To: Michelle Brot

Subject: Fw: Zee pig protocol

fyi

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To: Molly K. Lucas <mklucas@uw.edu>
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Subject: Re: Zee pig protocol

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Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu
206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 3:49 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu>

Subject: Zee pig protocol

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Maybe we can both go through it and compare notes?

Thanks, Molly From: Gary Fye <gfye@u.washington.edu>

To: Nick Reyes <nlreyes@uw.edu>, Brian Iritani <biritani@uw.edu>

Sent: 7/3/2020 1:19:07 PM

Subject: Fwd: new R01 grant for Liu - MRI

FYI...looking to get rolling at ARC by the end of the year.

Gary

----- Forwarded message -----

From: **Zi-Jun Liu** <<u>zjliu@uw.edu</u>> Date: Fri, Jul 3, 2020 at 12:27 PM Subject: Re: new R01 grant - MRI To: Gary A. Fye <<u>gfye@uw.edu</u>>

Gary,

This is an anther good resource. I will contact the contact person to see the availability of the use for minipigs.

This project will use the total of 30 18-month-old Yucatan minipigs with either genders, 10 for Aim 1 (normal ones) and 20 for Aim 2 (10 normal for tongue base volume reduction and 10 obese for tongue base volume enlargement.

Zee

From: Gary Fye <gfye@u.washington.edu>

Sent: Friday, July 3, 2020 10:44 AM
To: Zi-Jun Liu <ziliu@uw.edu>
Cc: Gary A. Fye <gfye@uw.edu>
Subject: Re: new R01 grant - MRI

Morning Zi,

There is an MRI for research in Health Sciences. See this link.

https://rad.washington.edu/research/equipment/

Also curious, how many pigs on your new project? You plan to use SPF or farm pigs?

Gary



Virus-free. www.avast.com

On Fri, Jul 3, 2020 at 9:30 AM Zi-Jun Liu <<u>zjliu@uw.edu</u>> wrote:

Just have one more question. Do you know if MRI scan on minipigs could be done in the main campus here? As you knew, we did these scans in the south campus, but the animal transportation has always been complicated and headache.

Thank you again,

Zee

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Friday, July 3, 2020 9:15 AM

To: Gary A. Fye <gfye@uw.edu>; Levin, Dmitry <dlevin@cardiology.washington.edu>

Subject: Re: new R01 grant - Fluoroscope Available?

Hello Gary,

Thank you so much for your quick reply and long-standing support on my research.

I would be much easier for me to carry out this experiment if it can be done in the ARC.

Dmitry, would you please confirm this as I am now preparing animal protocol and needing this info.

Thank you very much,

Zee

From: Gary Fye <gfye@u.washington.edu> Sent: Thursday, July 2, 2020 3:30 PM

To: Zi-Jun Liu <zjliu@uw.edu>; Levin, Dmitry <dlevin@cardiology.washington.edu>

Cc: Gary A. Fye <gfye@uw.edu>

Subject: Re: mew R01 grant - Fluoroscope Available?

Afternoon Zi.

Congrats on your new grant!

I have added Dmitry Levin who does have a fluoroscope here in Health Sciences. I believe it is available for rent with him running the machine but he can elaborate. DCM can run the anesthesia for the pig at ARC and the machine is portable so can be moved there.

Let me know if you need any other assistance and have a good weekend.

Gary

On Thu, Jul 2, 2020 at 2:19 PM Zi-Jun Liu <<u>zjliu@uw.edu</u>> wrote: Hello Gary,

My new R01 will be funded by the NIDCR soon and I am now preparing the animal protocol. One major procedure for this new project is to take x-ray fluoroscopy on live minipigs during swallowing with barium and respiration. I remembered that you mentioned that the Vet Services may have the machine in the facility. Would you please let me know if I can do this in the animal facility by then (late this year) , or this procedure will have to be performed in the South Lake campus as I did previously?

Thank you very much,

Zee

--

Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington

Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington



Virus-free. www.avast.com

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Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington

| | Activity | Author | ▼ Activity Date | |
|--------------------|---|-----------------------|-------------------|--|
| 4 | Congruence Letter Attached | Brot, Michelle | 9/1/2020 10:00 AM | |
| ₫ eGC1 | 因 eGC1 A146864-Approval.pdf | | | |
| 1 | Letter Sent | Brot, Michelle | 9/1/2020 9:59 AM | |
| ☐ Corres | pondence_for_PROTO202000105.doc | | | |
| B | Letter Prepared | Brot, Michelle | 9/1/2020 9:58 AM | |
| | pondence_for_PROTO202000105.doc | | | |
| | Approval Period Edited | Brot, Michelle | 9/1/2020 9:56 AM | |
| \subseteq | Designated Member Review Submitted | Burich, Andrew J | 9/1/2020 8:47 AM | |
| → | Response Submitted | Liu, Zi-Jun | 8/31/2020 4:02 PM | |
| 0 | Clarification Requested by IACUC Member | Administrator, System | 8/31/2020 2:21 PM | |
| Sending this | submission back to clarifications to address questions sent via email. | | | |
| 4 | Clarification by Designated Reviewer Requested | Huang, Stephanie W | 8/31/2020 2:21 PM | |
| Sending this | submission back to clarifications to address questions sent via email. | | | |
| → | Response Submitted | Liu, Zi-Jun | 8/31/2020 9:12 AM | |
| Hello Michel | le, | | | |
| The question | ns raised by the committee during the 2nd review have been addressed and relevant revision have been made. | | | |
| Thank you, | | | | |
| Zee | | | | |
| 0 | Clarification Requested by IACUC Member | Administrator, System | 8/28/2020 3:48 PM | |
| Please see thanks. | further clarifications needed. Some requests were not completed and there was a question about the new procedure fo | or the high fat diet. | | |
| 4 | Clarification by Designated Reviewer Requested | Burich, Andrew J | 8/28/2020 3:48 PM | |
| Please see thanks. | further clarifications needed. Some requests were not completed and there was a question about the new procedure fo | or the high fat diet. | | |
| → | Response Submitted | Liu, Zi-Jun | 8/28/2020 3:03 PM | |
| Hello Miche | Hello Michelle, | | | |
| Thank you f | or sending me the comments/questions by the committee. | | | |
| | | | | |

All comments/questions have been addressed and the protocol has been revised accordingly.

Hope the approval will be coming soon,

Zee

| Hello, | | | |
|-------------------------|--|--|---|
| The IACUC | had additional questions regarding this submission. Please revise/respond as needed and submit back to our office. | | |
| Thank you, Stephanie | | | |
| 4 | Clarification by Designated Reviewer Requested | Huang, Stephanie W | 8/28/2020 10:44 AM |
| Hello, | | | |
| The IACUC | had additional questions regarding this submission. Please revise/respond as needed and submit back to our office. | | |
| Thank you, Stephanie | | | |
| å.+ | Designated Reviewers Assigned | Huang, Stephanie W | 8/28/2020 10:43 AM |
| * | Assigned to Designated Review | Huang, Stephanie W | 8/28/2020 10:42 AM |
| Û | Agenda Item Removed | Huang, Stephanie W | 8/28/2020 10:42 AM |
| > | Private Comment Added | Burich, Andrew J | 8/26/2020 2:30 PM |
| I have sever | ral comments | | |
| \$ | Tags Managed | Williams, Ashley E | 8/26/2020 11:31 AM |
| Niranjan Ba | lu removed | | |
| Ф | Tags Managed | Stocking, Kim | 8/26/2020 7:53 AM |
| 9 | Private Comment Added | Stocking, Kim | 8/25/2020 3:35 PM |
| I reviewed th | nis and adding a comment. | | |
| Ω | Comment Added | Liu, Zi-Jun | 8/24/2020 8:58 PM |
| Please remo | ove Niranjan Balu from the protocol. | | |
| Thanks, | | | |
| Zee | | | |
| Ω | Comment Added | Williams, Ashley E | 8/24/2020 4:50 PM |
| REMINDER | : I am unable to approve Niranjan Balu on your protocol due to incomplete training. Please have Niranjan complete all | required training. If you believe this is an error, please | send us verification of completed training. |
| | g needs to be completed: I Use Laws & Regulations. Copy and paste the following link (https://depts.washington.edu/auts/courses/courses_onlin | ne.html) to take the course. | |
| For addition | al information please visit the Animal Use Training website at: http://depts.washington.edu/auts/requirements.html | | |
| 8 | Ancillary Review Submitted | Cashman, Judy L | 8/24/2020 2:06 PM |
| iei es | Ancillary Reviews Managed | Cashman, Judy L | 8/24/2020 2:06 PM |
| | | | |
| | | | |

Administrator, System

Clarification Requested by IACUC Member

8/28/2020 10:44 AM

| A 200 MO | Activity | Author | ▼ Activity Date |
|---|---|--------------------|--------------------|
| \$ | Tags Managed | Cashman, Judy L | 8/24/2020 2:06 PM |
| 4 0 | OHRs attached | Cashman, Judy L | 8/24/2020 2:05 PM |
| | Meeting Assigned | Brot, Michelle | 8/20/2020 1:36 PM |
| Ø | Pre-Review Submitted | Brot, Michelle | 8/20/2020 1:35 PM |
| → | Response Submitted | Liu, Zi-Jun | 8/20/2020 1:33 PM |
| Michelle, | | | |
| This last ques | stion has been addressed. | | |
| Thank you, | | | |
| Zee | | | |
| 4 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/20/2020 1:30 PM |
| Hi Zee, The vet had o | one last suggestion that you will need to confirm or modify. | | |
| Thanks, Mich | elle | | |
| → | Vet Consult Submitted | Lucas, Molly K | 8/20/2020 12:18 PM |
| Do you accep Does not nee | Do you accept the submission? yes Does not need vet re-review unless there is a veterinary question (assuming my final edits are retained) | | |
| ~ | Vet Consult Sent | Brot, Michelle | 8/19/2020 10:51 AM |
| Zee has edite | d the surgery procedures to include more information about the sutures. | | |
| → | Response Submitted | Liu, Zi-Jun | 8/19/2020 10:45 AM |
| Michelle, | | | |
| The revisions | have been made in both survival surgeries by following the recommendation from the Vet Services. | | |
| Thank you, | | | |
| Zee | | | |
| 47 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/19/2020 10:12 AM |
| HI Zee, The vet had a | a follow-up question about your sutures, and also note that you still need to add additional information for the Imp | lantation surgery. | |
| → | Vet Consult Submitted | Lucas, Molly K | 8/19/2020 8:51 AM |
| Do you accept the submission? no Getting close but need some more info in surgeries | | | |
| * | Vet Consult Sent | Brot, Michelle | 8/18/2020 11:27 AM |
| | | | |

| → | Response Submitted | Liu, Zi-Jun | 8/18/2020 10:32 AM |
|-------------------------|---|--|--|
| Michelle, | | | |
| The two que | stions from Vet Services have been addressed and the revisions have been made accordingly. | | |
| Thank you, | | | |
| Zee | | | |
| 7 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/18/2020 9:53 AM |
| Hi Zee, The | vet had one additional question and a comment. | | |
| } | Vet Consult Submitted | Lucas, Molly K | 8/18/2020 9:01 AM |
| | pt the submission? no esponse re: masseter approach | | |
| 4 | Vet Consult Sent | Brot, Michelle | 8/17/2020 11:14 PM |
| Questions w | ere addressed. | | |
| → | Response Submitted | Liu, Zi-Jun | 8/17/2020 7:44 PM |
| Michelle, | | | |
| did respond | d to this question by revising the procedures for catheter and EMG wires. | | |
| The catheter | r will be sutured to the nearby skin of the nose. After recording, the catheter will be removed without further a | nesthesia as did for the previous recording of natural | sleep in minipigs. |
| Zee | | | |
| 5 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/17/2020 12:46 PM |
| Hi Zee, There is one | part of a question from the vet that you still need to answer: | | |
| 'Please edit | to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure | exactly where the sutures might be placed" | |
| | led to the guestion about whether anesthesia will be required to remove the sutures but you didn't include an | | Please add this information to the procedure |
| - San Goponia | Response Submitted | Liu, Zi-Jun | 8/17/2020 10:13 AM |
| 7 | | | |
| Michelle, | | | |
| have addre | assed all comments/questions by the secondary review from the Vet Services. I hope this would make the pro- | cess move forward. | |
| Thank you, | | | |
| Zee | | | |
| (| Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/17/2020 8:52 AM |
| Hi Zee, Please addre | ess the follow-up questions from the vet. Looks like we're getting close now! | | |
| Thanks, Micl | helle | | |
| → | Vet Consult Submitted | Lucas, Molly K | 8/16/2020 1:30 PM |
| | ept the submission? no | | |
| will review re | esponses | | |
| | | | |
| | | | |
| | | | |

III review responses Brot, Michelle 8/11/2020 10:25 AM Vet Consult Sent Hi Molly, I checked through the responses and most of them were there although I'll let you decide about the quality. I had Zee do a couple items that he had overlooked and now those seem to be included as you requested. Thanks, Michelle **→** Response Submitted Liu, Zi-Jun 8/11/2020 9:16 AM Michelle, I did some revisions in the two surgeries per your instruction. I tired to remove Niranjan Balu, Daniel Leotta, and Jeffrey Thiel from all substance administration and post-op analgesic plan, but it does not look successful. Would you please help on this? Thank you very much for your prompt replies and helps always, Zee Brot, Michelle 8/10/2020 10:59 PM 4 Clarification by Pre-Reviewer Requested Hi Zee, Please make the change to create the Fentanyl patch and Carprofen procedures and add them to the surgeries, as requested by the vets, and as detailed in my e-mail to you. Liu, Zi-Jun 8/10/2020 11:24 AM Response Submitted **→** Michelle, All question from the review of Vet Services have been addressed and the protocol has been revised accordingly.

Zee

| | Activity | Author | * Activity Date |
|-------------------------|--|--------------------|--------------------|
| 47 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/7/2020 4:49 PM |
| Hi Zee, | | | |
| Please add | ress the vet's comments and questions. Let me know if you have any difficulty making the edits. | | |
| Have a nice | e weekend, Michelle | | |
| 90 | Private Comment Added | Lucas, Molly K | 8/7/2020 10:46 AM |
| MB, as we | discussed, anesthesia personnel still needs editing (just a reminder) | | |
| → | Vet Consult Submitted | Lucas, Molly K | 8/7/2020 10:45 AM |
| Do you acc Needs vet | ept the submission? no re-review | | |
| 9 | Private Comment Added | Williams, Ashley E | 8/5/2020 9:31 AM |
| Training rea | minder sent to N. Balu 8/5/20 | | |
| ~ | Vet Consult Sent | Brot, Michelle | 8/4/2020 3:23 PM |
| I believe th | is is now ready for your review, Molly. Thanks! | | |
| -> | Response Submitted | Liu, Zi-Jun | 8/4/2020 1:41 PM |
| | | | |
| Michelle, | | | |
| The Vet ad | ministered anesthetic procedure has been added. | | |
| Thank you, | | | |
| Zee | | | |
| 4 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 8/4/2020 12:57 PM |
| Please add | the Anesthesia procedure you discussed with the vets. | | |
| → | Vet Consult Submitted | Lucas, Molly K | 7/28/2020 11:52 AM |
| Do you acc | ept the submission? no | | |
| Q | Comment Added | Lucas, Molly K | 7/27/2020 4:31 PM |
| Vet service | /et services has contacted Dr. Liu to arrange a meeting to discuss anesthesia for this protocol. Please meet and edit in Hoverboard as needed per what is agreed upon in that meeting. | | |
| production (| Vet Consult Sent | Lucas, Molly K | 7/27/2020 4:29 PM |
| \$ | Tags Managed | Brot, Michelle | 7/27/2020 2:09 PM |
| 4 | Vet Consult Sent | Brot, Michelle | 7/27/2020 2:07 PM |
| Zi-Liu has r | Zi-Liu has received a grant and has resurrected his minipig protocol. Please prioritize this as the funding agency is waiting for its approval. Nick is very familiar with Zee's procedures and also, Zee e-mailed Gary Fye and asked him to review he Anesthesia procedure description to make sure it sounds consistent with what Vet Services does. | | |

the Anesthesia procedure description to make sure it sounds consistent with what Vet Services does.

| de. | | | | |
|---------------------------|--|---|---|----------------------|
| Hello Mich | elle, | | | |
| | wered all of your new questions and made relevant changes per your instruction, vere actually made.Today, I first listed each procedure and click the "edit" button c | | | ast time but no |
| Thank you | very much, | | | |
| Zee | | | | |
| 4 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 7/27/2020 12:19 AM | |
| Hi Zee, We're getti | ing closer nowjust a few more questions to finish and I can pass this on to the | vets for their review. Let me know if you need help. | | |
| Regards, Michelle | | | | |
| → | Response Submitted | Liu, Zi-Jun | 7/23/2020 10:16 AM | |
| Michelle, | | | | |
| Thank you | for quick review again. I hope all of your questions have been addressed appropriate | riately in this revision. | | |
| Zee | | | | |
| | Clarification by Pre-Reviewer Requested | Brot, Michelle | 7/22/2020 2:35 PM | |
| Hi Zee, I h need help. | ave reviewed your changes and the protocol is much better now. There are some Please be sure to address the question both in the text and then in your respons | additional questions for you, but I believe you are more experienced at Ho se so I know what changes you made. | verboard and can make the changes on your own. I am a | available if you |
| > | Response Submitted | Liu, Zi-Jun | 7/21/2020 9:57 AM | |
| h | Clarification by Pre-Reviewer Requested | Brot, Michelle | 7/20/2020 1:55 PM | |
| Sending it | back to you for changes. | | | |
| → | Response Submitted | Liu, Zi-Jun | 7/20/2020 12:55 PM | |
| h | Clarification by Pre-Reviewer Requested | Brot, Michelle | 7/15/2020 5:02 PM | |
| | anks for updating the Q5 sections and providing a timeline for your procedures. I Good luck! ~Michelle | here are still quite a few updates and procedures you need to work on to m | ake this a complete protocol. Let me know if you need h | elp or clarification |
| • | Private Comment Added | Williams, Ashley E | 7/15/2020 2:07 PM | |
| Sent N. Ba | alu reminder 7/8 | | | |
| → | Response Submitted | Liu, Zi-Jun | 7/15/2020 10:55 AM | |
| 17 | Clarification by Pre-Reviewer Requested | Brot, Michelle | 7/13/2020 3:16 PM | |
| Hi Zee, Please add | dress the questions, carefully editing the protocol according the the suggestions. | Contact me if you need assistance. Regards, Michelle | | |
| leŭ M | Ancillary Reviews Managed | Lim, Amy | 7/13/2020 9:41 AM | |
| ¢ | Tags Managed | Lim, Amy | 7/13/2020 9:41 AM | |
| | | | | |
| | | | | |
| | | | | |

Liu, Zi-Jun

Response Submitted

7/27/2020 10:44 AM

| | Activity | Author | ▼ Activity Date | |
|----------------|--|----------------------|-------------------|--|
| Jos. | Ancillary Reviews Managed | Kunsman, Robyn | 7/13/2020 8:27 AM | |
| Q | Tags Managed | Kunsman, Robyn | 7/13/2020 8:27 AM | |
| ٥ | Tags Managed | Williams, Ashley E | 7/8/2020 10:49 AM | |
| PI completed | AUMS | | | |
| &+ | Coordinator Assigned | Jimenez, Selesteen | 7/7/2020 10:17 AM | |
| Assigned to N | Michelle Brot | | | |
| Ø | Assigned Portfolio ID | Jimenez, Selesteen | 7/7/2020 10:17 AM | |
| Ф | Tags Managed | Jimenez, Selesteen | 7/7/2020 10:17 AM | |
| Hold for PI au | ums | | | |
| | Balu expired l&r ☐ Action Required for AUMS #3393-05.pdf | | | |
| 0 | Submitted | uwhover | 7/7/2020 8:32 AM | |
| Submitting or | n behalf of the PI. Please assign to Michelle for review. | | | |
| * | Protocol Created | uwhover | 7/2/2020 1:02 PM | |
| Copied from | PROTO201600409 3393-04: Obstructive Sleep Apnea – An Obese Minipíg Model | | | |
| 83 items | | page 4 of 4 | 25 / page | |

From: Leandra Mosca lmosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/5/2020 3:14:52 PM Subject: Liu Pig Anesthesia

Attach: [Liu First Draft anesthesia recommendations.docx]

Hi Nick,

I have attached my summary/recommendations for the Liu pig project.

The pigs do not need sedation or restraint for removing equipment after recording—I confirmed with Zee.

Should we discuss this when you are available?

Thanks, Leandra

Leandra Mosca, DVM
Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772



New Project

Aim 1 (6 weeks)

- 1. Imaging: MRI, EUS, and videofluoroscopic swallowing examination (VFSE)
 - a. MRI and Ultrasound: twice; VFSE: 6 times
 - b. 30 min for MRI, 5-10 min for Ultrasound, and 15-20 min for SVF
 - c. No intubation
 - d. Swallowing: new part, live recording during mastication
 - e. Days 19 and 34, hooked up to instrumentation (10-15 min), wake up for recording session
 - f. Recommendations:
 - i. Option 1: Induce and maintain with mask on isoflurane 4-3% (keep endotracheal tube nearby in case of emergency- especially if this entire process goes longer than anticipated).
 - ii. Option 2: Propofol CRI 11 mg/kg/h or alfaxolone CRI 13 mg/kg/hr IV
 - 1. May begin with isoflurane/intubation and transition to TIVA CRI once stable or utilize combination of both
 - iii. (Used in past studies) GKX CRI at 2.2ml/kg/hr (combined): Guaifenesin 50 mg/ml +Ketamine 100mg/ml 2.2 ml/kg/hr + Xylazine 100mg/ml 2.2 lV
- 2. Implantation (Survival Surgery)
 - a. The implants include: 1) 8 SONO crystals in the tongue base with a skin button, 2) 8 pairs of 0.1mm wire EMG electrodes with a micro-connector, and 3) 6 metal balls and 3 miniscrews.
 - b. 2.5 hours, intubated
 - c. Submandibular incision along the midline
 - d. Recommendations:
 - i. Pre-medication: Ketamine/xylazine 5.0 mg/kg/2.0 mg/kg + butorphanol 0.2 mg/kg all IM (torb for muscle relaxation). Potent anesthesia and smooth recovery important for these animals and tongue base reduction (see below).
 - ii. After sedation sets in induce with isoflurane mask at 3-4% and intubate when ready (loss of jaw tone, ventral rotation of eye, prolapsing third eyelid).

Aim 2 (7-8 weeks)

- 1. Imaging: MRI, EUS, and videofluoroscopic swallowing examination (VFSE)
 - a. See above
- 2. Tongue base reduction surgery (Survival surgery)
 - a. Coblation, 20mm midline incision 20mm posterior to circumvallate papillae
 - b. 11 days after implantation
 - c. Immediately after coblation, SONO measurements will be taken and the actual volumetric decrease will be calculated using SonoVol. The entire surgery will take 1 to 1.5 hours

d. Recommendations:

- i. Pre-medication: Ketamine/xylazine 5.0 mg/kg/2.0 mg/kg + butorphanol 0.2 mg/kg all IM(torb for muscle relaxation). Potent anesthesia and smooth recovery important for these animals and tongue base reduction (see below).
- ii. After sedation sets in induce with isoflurane mask at 3-4% and intubate when ready (loss of jaw tone, ventral rotation of eye, prolapsing third eyelid).

From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Monday, August 24, 2020 3:19 PM
To: Molly K. Lucas; Michelle Brot
Subject: Liu Pig Swallowing Protocol

Hey there,

Before I ask the PI this question, I thought maybe you could help me out.

This is for Aim 1, but may apply to Aim 2: I noticed that in **Survival Surgery: Liu-Minipig: Implantation (Team)** he lists on pg2, Q4 a procedure for Vet Services Administered Anesthetics. However, this is completely different than **Substance Administration: Liu-Minipig: Anesthesia Protocol (Team)** that is in the Procedure List.

Which is correct? The one in the survival surgery procedure needs to be edited because it talks about sleep devices.

I¹d like to ³thank² the person that assigned me this protocol. ☺

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA

Director, Animal Resources
Benaroya Research Institute at Virginia Mason
1201 Ninth Avenue | Seattle, WA 98101
p 206.342.6967
BenaroyaResearch.org

⁻⁻CONFIDENTIALITY NOTICE--: The information contained in this email is intended for the exclusive use of the addressee and may contain confidential information. If you are not the intended recipient, you are hereby notified that any form of dissemination of this communication is strictly prohibited. www.benaroyaresearch.org

| New R01 grant - Anesthesia for Liu Pigs □□□□□ | |
|---|-----|
| ZL | |
| Zi-Jun Liu <zjliu@uw.edu> Tue 8/4/2020 12:53 PM</zjliu@uw.edu> | |
| | |
| | |
| To: | |
| Nicholas L. Reyes; Michelle Brot | |
| Cc: | |
| achris08; Leandra Mosca; Gary A. Fye; Molly K. Lucas; VET SERVICES PROTOCOL REVIEW | |
| Hello Nick and Michelle, | |
| Nick, thank you so much for your quick helps on the anesthetic procedure. Does this indicate that the Vet Services Protocol Review has been completed? | |
| Michelle, would you please unlock the protocol, so I can add " <u>Vet Services Administered</u> <u>Anesthestics</u> " as a new procedure? | |
| Thank you again, | |
| Zee From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Tuesday, August 4, 2020 11:52 AM To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>; Zi-Jun Liu <zjliu@uw.edu> Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu <gfye@uw.edu="" a.="" fye="" gary="">; Molly K. Lucas <mklucas@uw.edu> Subject: Re: New R01 grant - Anesthesia for Liu Pigs</mklucas@uw.edu></lmosca@uw.edu></achris08@uw.edu></mbrot@uw.edu></zjliu@uw.edu></vsreview@uw.edu></nlreyes@uw.edu> | ı>; |

Hello Zee,

I touched base with Michelle Brot regarding the best way to add in our anesthetic plan for your protocol. Because VS will be running and maintain anesthesia for all of your experiments you can go ahead and add our pig anesthesia attachment document. This includes way more anesthetic options than we are likely to use but gives us the flexibility to adjust based on our experiences. I've attached the current version of this doc to this email. Leandra is still working on our specific plan for your experiments, but we will keep that version internal for our preparation for you experiments in the fall or winter. Below are instructions from Michelle on how to add this anesthetic procedure into hoverboard. Please let her know if you have any questions regarding wording.

Add a procedure called "<u>Vet Services Administered Anesthestics</u>" which refers to an attachment at the end of the procedure that lists all potential anesthetics that may be used in a surgery or other procedure for that species. Here is what it says in Herring's Q2 "Describe step-by-step the procedure for administering the substance(s):" for the anesthetics administration procedure "Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended."

Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Wednesday, July 29, 2020 8:39 AM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>;

Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Please see the zoom invitation below for tomorrow at 10AM. Looking forward to meeting you.

Best,

Alex

DCM is inviting you to a scheduled Zoom meeting.

Join Zoom Meeting

https://washington.zoom.us/j/

Meeting ID:

One tap mobile

+12063379723,, # US (Seattle) +12532158782,, # US (Tacoma)

Dial by your location

- +1 206 337 9723 US (Seattle)
- +1 253 215 8782 US (Tacoma)
- +1 971 247 1195 US (Portland)
- +1 213 338 8477 US (Los Angeles)
- +1 346 248 7799 US (Houston)
- +1 602 753 0140 US (Phoenix)
- +1 669 219 2599 US (San Jose)
- +1 669 900 6833 US (San Jose)
- +1 720 928 9299 US (Denver)
- +1 470 250 9358 US (Atlanta)
- +1 470 381 2552 US (Atlanta)
- +1 646 518 9805 US (New York)
- +1 646 876 9923 US (New York)
- +1 651 372 8299 US (St. Paul)
- +1 786 635 1003 US (Miami)
- +1 267 831 0333 US (Philadelphia)
- +1 301 715 8592 US (Germantown)
- +1 312 626 6799 US (Chicago)

Meeting ID:

Find your local number: https://washington.zoom.us/u/aADpJbh5Q

Join by SIP

@zoomcrc.com

Join by H.323

162.255.37.11 (US West)

162.255.36.11 (US East)

221.122.88.195 (China)

115.114.131.7 (India Mumbai)

115.114.115.7 (India Hyderabad)

213.19.144.110 (EMEA)

103.122.166.55 (Australia)

RCW 42.56.420(4)

209.9.211.110 (Hong Kong SAR) 64.211.144.160 (Brazil) 69.174.57.160 (Canada) 207.226.132.110 (Japan)

Meeting ID:

RCW 42.56.420(4)

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Tuesday, July 28, 2020 9:21 PM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>;

Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Alex,

Yes, please send me the meeting invitation.

Thanks,

Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 28, 2020 4:42 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thanks for getting back to us. Can you meet this Thursday at 10AM via zoom?

Thanks,

Alex

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Monday, July 27, 2020 9:34 PM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>;

Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Alex,

Thanks for your mail. I am pretty flexible this week for a Zoom meeting to discuss the anesthetic procedures for my new project. Please let me know when the meeting will be set up.

Looking forward to getting your helps with anesthetic procedures.

Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Monday, July 27, 2020 4:43 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hi Zee,

Just wanted to follow up with you about discussing your anesthesia plan for your new protocol.

Can you reply with your availability so we can arrange zoom meeting to discuss?

Thank you, Alexandra Christodoulou, DVM Veterinary resident

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 21, 2020 3:00 PM

To: Zi-Jun Liu <ziliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>;

Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thank you for reaching out to vet services for protocol review. Dr. Nick Reyes, Dr. Leandra Mosca, and myself would like to set up a Zoom meeting to discuss your anesthetic plan for the minipigs in your new protocol.

Do you have time later this week on either Thursday or Friday to talk with us?

And please don't hesitate to let me know if you have any additional questions.

Best, Alex

Alexandra Christodoulou, DVM Veterinary Resident

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Tuesday, July 21, 2020 10:29 AM

To: Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Gary,

Great, Thank you so much,

Zee

From: Gary Fye <gfye@u.washington.edu> Sent: Tuesday, July 21, 2020 10:17 AM

To: Zi-Jun Liu <zjliu@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Morning Zi,

I have added our protocol review to this email. A veterinarian will contact you to discuss the anesthesia for your project.

Thanks, Gary

On Tue, Jul 21, 2020 at 10:12 AM Zi-Jun Liu <<u>ziliu@uw.edu</u>> wrote:

Hello, Gary,

Thank you for providing info about MRI and x-ray C-Arm machine.

I am working on the animal protocol with IACUC. I have been using the anesthetic procedures created by the Vet Service for my previous project on OSA obese minipigs. Would you please let me know who I should ask for reviewing these anesthetic procedures or if you would be able to review them?

Best regards,

Zee

Q #3 at the bottom of the page: Re: the statement, "The interval between the two surgeries is 11 days." I recommend editing for a bit more flexibility just in case something happens and the interval is slightly different. It would be fine to say something like "at least 10 days."

Please comment/edit as needed.

Exp 1 and Exp 2, Q #5: These timelines are very helpful. I recommend editing to include some flexibility in timing (e.g., adding "approximately" in some places), just in case something unexpected happens.

Exp 1 and Exp 2, Q #7: Please edit to include the frequency that the pigs will be checked by protocol personnel (e.g., at least 3x/wk). Fyi, I edited to include the post-op monitoring (twice a day for 5 days after surgery, as listed in the surgery procedure).

Liu-Minipig: Food restriction, Q #3 states, "No more than 24 hr will elapse between feedings"; however, Q #2 states, "Provide the maximum number of hours food/fluid will be restricted: 16." Please edit to correct this inconsistency.

Implants: Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers (Team): This procedure includes the text, "Identify criteria under which animals will be removed from research: Uncontrolled infection or > 20% loss of body weight." Please edit to include this in Q #7 of the Experiments as euthanasia criteria, so that this information is listed consistently throughout the protocol.

Implants: Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers (Team), Q #5: Please edit to remove the copied surgery details and replace it with a simple statement such as "please refer to survival surgery." That way if changes are made to the surgery, changes only need to be made in one procedure, and this helps avoid inconsistencies.

Liu-Minipig: Baseline recording:

- -Re: "After 10-15' of feeding on the barium diet, sensors and wire electrodes will be removed, and the pig will return to its pen." Is this 10-15 minutes? Please edit to clarify.
- -Please edit to include the purpose of the red rubber catheter and to remove the size (#10), as you may need different sizes for different size pigs.
- -I'm not sure I understand the part about replacing the mask with the red rubber catheter. Vet services is under the impression that inhalant anesthesia (e.g., isoflurane) delivered by mask can be used for all of the imaging procedures. Is this correct?

Other: Liu-Minipig: Longitudinal tracking (Team): Re: "In each recording session, non-working SONO crystals or EMG electrodes will be replaced if necessary." This is not consistent with the Implant procedure (Q #7), which states, "If some SONO crystals fail, we may re-implant them only during the terminal recording, and the number will be limited less than 4 crystals." The implant procedure does not address re-implantation of EMG electrodes one way or the other.

It sounds like replacement of crystals or EMG wires would be a relatively invasive procedure (another surgery), so I think the plan of only performing replacement as a terminal procedure sounds best. I think it would be a good idea to edit Q #5 of the experiments to state that the terminal surgery may be done at an earlier timepoint if instrumentation fails, unless this would not be done. Addition of a repair survival surgery would require strong scientific justification and would need to be included in the multiple survival surgery table.

Please comment/edit as needed.

Liu-Minipig: Terminal recording and stimulation session, Re: the statement, "After the completion of the stimulation session, the pig will be euthanized by cardiac injection of over-dosed phenobarbital." I edited this to say simply that the pig will be euthanized with pentobarbital (not phenobarbital, and it may be given IV rather than intracardiac). No action necessary on your part if you are amenable to this edit, otherwise further edit as needed.

Liu-Minipig: Terminal recording and stimulation session: Please create a non-survival surgery procedure and move the appropriate information from this procedure to that procedure (the part beginning with, "After this recording, the pig will be re-anesthetized, placed supine, and the bilateral hypoglossal nerve complex, including nerve trunk (HG), and its medial (HGM) and lateral (HGL) branches, genioglossus (GG), and stylogossus (SG) will be exposed and isolated through a submandibular approach.").

Special Diet: Soft diet (Team), Re: "Water mixed with regular pig pellet with the ratio of 4:6.," this is very specific. Please edit to remove the precise ratio for increased flexibility.

Substance Administration: Liu -Minipig: Bromodeoxyuridine (BrdU) Administration (Team)

And

Substance Administration: Liu-Minipig: Fluorochrome Labels for Bone (Team):

Will the the animals be anesthetized when IV injections are performed? Is a catheter placed? It looks like many (but not all) of the timepoints for IV injection coincide with other anesthetic events. In Exp 1, the fluorochrome injection given 7 days prior to the terminal procedure does not appear to coincide with another planned anesthetic event. In Exp 2, the BrdU given 15 days before the endpoint does not appear to coincide with another planned anesthetic event, in addition to the fluorochrome 7 days prior.

If these will be an additional anesthetic events, this should be made clear in the timeline (Q #5 of the Experiment), and anesthesia should be included in the BrdU and fluorochrome substance administration procedures.

Please comment/edit as needed to clarify how IV administration will be performed.

Survival Surgery: Liu-Minipig: Implantation (Team) Re: the statement, "If the infection becomes severe and out of control, the major implants (skin button and micro-connector) will be removed." This seems inconsistent with the response to Q #4ii of this procedure, which is "Identify criteria under which animals will be removed from research:

Uncontrolled infection and > 20% loss of body weight after the procedure." And the implant procedure states "No removing implants. If some SONO crystals fail, we may re-implant them only during the terminal recording,...".

Please edit as needed to ensure that the plan is described consistently throughout the protocol/procedures.

Survival Surgery: Liu-Minipig: Implantation (Team)

-Q #4: Please edit to include a post-op analgesic plan for this surgery. Dr. Reyes and I discussed this, and we recommend 72 hr of opioid (one dose of SR buprenorphine or multiple doses of regular buprenorphine or fentanyl patch) and 72 hr of NSAID (e.g., carprofen 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr). There is a Yucatan standard procedure for 72 hr regular or SR buprenorphine, so I added this for you, but it looks like you will need to create and add procedures for the Fentanyl patch (for dose say that vet services will determine correct patch size/dose) and the Carprofen, as well as edit to incorporate the analgesic plan into the post-op monitoring section, if you are amenable to this plan.

-Q #5: This part is for monitoring during surgery – e.g., Vet services will monitor HR, body temperature, respiratory rate, blood pressure, oxygen saturation. Please edit as needed to address the question. Please move the language currently in Q #5 to Q #6 and expand on it a bit (e.g., TPR, attitude, activity level and appetite will be assessed; TPRs may be discontinued after the first day post-op check at vet service's discretion).

Survival Surgery: Liu: Tongue base reduction surgery (Team):

- -Q #4: Please edit to include a post-op analgesic plan for this surgery. Dr. Reyes and I discussed this, and we recommend 72 hr of opioid (one dose of SR buprenorphine or multiple doses of regular buprenorphine or fentanyl patch) and 72 hr of NSAID (e.g., carprofen 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr). There is a Yucatan standard procedure for 72 hr regular or SR buprenorphine, so I added this for you, but it looks like you will need to create and add procedures for the Fentanyl patch (for dose say that vet services will determine correct patch size/dose) and the Carprofen, as well as edit to incorporate the analgesic plan into the post-op monitoring section, if you are amenable to this plan.
- -Q #5, Please edit to include more details, e.g., something like Vet services will monitor HR, body temperature, respiratory rate, blood pressure, oxygen saturation.
- -Q #6, Please edit to include more details, e.g., something like TPR, attitude, activity level and appetite will be assessed; TPRs may be discontinued after the first day post-op check at vet service's discretion

-Q #7: Please edit to include more detail. E.g., the text included here in the other surgery is, "When the pig loses its appetite and is reluctant to move around. Pain medication and antibiotics will be given per the instruction of Vet Services."

Prophylactic antibiotics for surgeries: I believe vet services recommended prophylactic antibiotics for the surgeries. VS recommends a single injection of Excede (ceftiofur) at the time of surgery. One injection at the time of surgery lasts for approx. 5 days. The dose is 2-5 mg/kg and it is given IM. If you are amenable to this recommendation, please create a Substance entry for it and add it to the surgeries.

Pig Sling use: I believe that potential use of a pig sling was discussed with vet services, but I don't see it mentioned anywhere in the protocol. If you are interested in potentially using a pig sling (e.g., as an option for some recording sessions as animals are recovering from anesthesia), please add this to the protocol. An "other" procedure is probably the best way to include this information. Training/acclimation should be included. Please contact vet services if you need help with this (vsreview@uw.edu).



APPROVAL OF NEW PROTOCOL SUBMISSION

September 1, 2020

Dear Zi-Jun Liu,

This email serves as written notice of animal use approval by the Institutional Animal Care and Use Committee (IACUC).

To help us better serve you, please take this <u>3 question survey</u> about your experience with the review process.

| Type of Review: | Designated Member Review |
|--------------------------|--|
| Short Title of Protocol: | 3393-05: Tongue Base in Respiration and Swallowing |
| Investigator: | Zi-Jun Liu |
| HoverBoard ID: | PROTO202000105 |

Please note the approval and expiration date listed. All animal use protocols must be renewed annually from the date of IACUC approval, independent of project or funding dates. Please refer to the assigned protocol number for all animal orders and future correspondence with the IACUC.

Protocol Approval Dates: 9/1/2020 to 8/31/2023.

Next Annual Expiration Date: 8/31/2021

Next Triennial Expiration Date: 8/31/2023

If you have any questions, contact OAWRSS at oawrss@uw.edu.

Sincerely

Office of Animal Welfare





Date: Thursday, November 5, 2020 8:46:07 AM

| Print Clo | S | E |
|-----------|---|---|
|-----------|---|---|

View: SF: Basic Information

Basic Information

1. * Select research team:

Liu, Z

2. * Title of protocol:

The Tongue Base in Respiration and Swallowing

3. * Short title:

3393-05: Tongue Base in Respiration and Swallowing

4. * Summary of research:

In this research, we propose to investigate the functional (respiration and swallowing) and morphological (spatial configuration of oropharynx) consequences of the volumetric alteration of the tongue base and to elucidate its reparative capacity through a study of its stem cell population - satellite cells. The overall hypothesis is that volumetric increase of the tongue base aids swallowing at the expense of oropharyngeal airway patency whereas volumetric decrease has the opposite effects. Further, we will establish the potential for myogenic repair of the tongue base by assessing its satellite cells in comparison to other skeletal muscles, and link these regenerative potentials to functional outcomes.

These studies aim to:

- 1) ascertain how tongue base behavior subserves respiration and swallowing
- 2) evaluate how tongue base volumetric changes affect respiration, swallowing, and the oropharyngeal space
- 3) assess healing after volumetric changes of the tongue base and to establish whether satellite cells in the tongue base enable myogenesis to repair muscle function.

The overall hypothesis is that volumetric increase of the tongue base aids swallowing at the expense of oropharyngeal airway patency whereas volumetric decrease has the opposite effects. The outcomes will lead to new understanding of how the tongue base participates in oropharyngeal function and dysfunction, and provide new knowledge about its muscle biology, wound healing, and functional recovery, which will help clinicians to develop better treatment strategies for oral cancers, OSA, and other oropharyngeal disorders.

5. * Principal investigator:

Zi-Jun Liu

6. * What is the intention of the animal protocol?

Experimental Research

Experimental Research Protocol Addition

1. * Will the protocol include breeding?

O Yes No

Protocol Team Members

1. Identify each additional person involved in the design, conduct, or reporting of the research:

| Name | Role | Involved in Animal Handling | Animale | l E-mail | Phone | |
|----------------------|-----------------------|--------------------------------------|---------|-----------------|---------------------------|---------------------------|
| | Student/Voluntee | ryes | no | | | FERPA RCW 42.56.070(1) |
| Sue Herring | Co-Investigator | yes | no | herring@uw.edu | +1 206 543- 3203 | |
| Daniel F Leotta | Research Scientist | no | no | leotta@uw.edu | +1 206 616- 6787 | |
| Katherin Rafferty | e Co-Investigator | yes | yes | kraff@uw.edu | +1 206 616- 9360 | |
| Vet Services | Other | yes | no | vsreview@uw.edu | (206) 583- 1853 | |
| Jeffrey Thiel | Research Scientist | no | no | jt43@uw.edu | +1 206 598- 6799 | |

2. If veterinary care will be provided by individuals outside of DCM or WaNPRC, provide the name, credentials and contact information below:

N/A

View: Custom SF: Funding Sources

Funding Sources

1. Identify each organization supplying funding for the protocol:

| | Funding Organization | eGC1 Number(s) |
|------|--|-------------------|
| View | National Institute of Dental and Craniofacial Research (NIDCR) | A146864 |

View: Custom SF: Scientific Aims

Scientific Aims

1. * Scientific aims of the research:

We propose to investigate the functional (respiration and swallowing) and morphological (spatial configuration of oropharynx) consequences of the volumetric alteration of the tongue base and to elucidate its reparative capacity through a study of its stem cell population - satellite cells. The overall hypothesis is that volumetric increase of the tongue base aids swallowing at the expense of oropharyngeal airway patency whereas volumetric decrease has the opposite effects. Further, we will establish the potential for myogenic repair of the tongue base by assessing its satellite cells in comparison to other skeletal muscles, and link these regenerative potentials to functional outcomes. The 1st Aim is to ascertain how tongue base behavior subserves respiration and swallowing; the 2nd Aim is to evaluate how tongue base volumetric changes affect respiration, swallowing, and the oropharyngeal space; and the 3rd Aim is to assess healing after volumetric changes of the tongue base and to establish whether satellite cells in the tongue base enable myogenesis to repair muscle function. The overall hypothesis is that volumetric increase of the tongue base aids swallowing at the expense of oropharyngeal airway patency whereas volumetric decrease has the opposite effects.

2. * Using language understandable to non-scientists, describe the goals and significance of the protocol to humans, animals and science:

The proposed study will shed light on how the tongue base functions in respiration and swallowing and the functional consequences following its volumetric reduction or enlargement. These outcomes will provide new in vivo information about the tongue base in oropharyngeal function and the functional, morphological, and histological consequences of volumetric changes. The success of this study will create a solid body of new knowledge about tongue base muscle biology, wound healing, and functional recovery to help clinicians to develop better treatment strategies for oral cancers, obstructive sleep apnea (OSA), and other oropharyngeal disorders.

3. * Provide a statement to address the potential harm to the animals on this study (e.g., pain, distress, morbidity, mortality) relative to the benefits to be gained by performing the proposed work:

The outcomes will demonstrate the tongue base function and malfunction in respiration and swallowing, and its capacity of regeneration.

While great benefits will be obtained from this project, the experimental approaches may have certain minor to moderate harm (pain and distress), to the animals, which include possible discomfort by wearing recording devices, multiple anesthetic sessions for x-ray imaging, surgeries or implantation and tongue base volume reduction, and potential infection during the longitudinal study due to implanted ultrasound crystals, ENG wire electrodes, and subcutaneous connector, which could lead to unexpected morbidity and/or mortality.

Experiments

Note: If you will be administering cells, cell lines, sera or other biologicals to rodents, contact the Rodent Health Monitoring Program (RHMP, rhmp@uw.edu). Testing may be required prior to administration to rodents.

1. * Define the experiments to be used in this protocol:

| Name | Species USD | A Coun | Count by tPain Category | Procedures | Husbandry Exception Types |
|---|----------------------------------|--------|-------------------------------|---|---|
| Aim 1: To ascertain how tongue base behavior subserves respiration and swallowing | Pigs - yes Yucatan Minipig | 10 | B: 0 C: 0 D: 10 E: 0 | ■ Euthanasia: Anesthetic Overdose, Pentobarbital or Pentobarbital Solution (Standard) ■ Food or Fluid Restriction: Liu- Minipig: Food restriction (Team) ■ Imaging: Liu- Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE) (Team) ■ Implants: Liu- Minipig: SONO crystals, wire EMG electrodes, and metal bone markers (Team) ■ Non-Survival Surgery: Liu- Minipig: Stimulation (Team) ■ Other: Liu- Minipig: Catheter and Wire Electrode (Team) ■ Other: Liu- Minipig: Use of pig sling (Team) ■ Other: Liu- Minipig: Baseline recording (Team) ■ Other: Liu- Minipig: Longitudinal tracking (Team) ■ Other: Liu- Minipig: Terminal | Pigs - Special/medicated diet Pigs - Food treats, as outlined in the policy, are not acceptable for part or all of the study. Pigs - Special/medicated diet |

recording (Team)

Name

Other: Liu-Minipig: Pig's training (Team) Other: Liu-

Minipig: Tongue impression (Team)

Special Diet: Liu-Minipig: Soft diet (Team)

Special Diet: Liu-Minipig: Barium diet (Team)

 Substance Administration: Analgesia, Buprenorphine or Buprenorphine SR (72 hours) (Standard)

Substance Administration: Liu-Minipig: Excede (ceftiofur) injection (Team)

Substance Administration: Liu-Minipig: Post-op analgesic plan (Team)

Substance Administration: Liu-Minipig: Fluorochrome Labels for Bone (Team)

Substance Administration: Liu-Minipig: Bromodeoxyuridine (BrdU) Administration (Team)

Substance Administration: Liu-Minipig: Anesthesia Protocol (Team)

Survival Surgery: Liu-Minipig: Implantation (Team)

Aim 2: To evaluate how volumetric changes of the tongue base affect respiration, swallowing, and

Pigs yes 20 Yucatan Minipig

B: 0 C: 0 D: 20

E: 0

Euthanasia: Anesthetic Overdose. Pentobarbital or Pentobarbital

Pigs -Special/medicated diet Pigs -

Special/medicated

Solution (Standard) water

Pigs - Food treats,

Count by Species USDA Count Pain Category

Procedures

as outlined in the blooks and eynot acceptable Types part or all of the study.

- Food or Fluid Restriction: Liu-Minipig: Food restriction (Team)
- Imaging: Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic
- swallowing examination (VFSE) (Team)
- Implants: Liu-Minipig: SONO crystals, wire EMG electrodes, and
- metal bone markers (Team)
- Non-Survival Surgery: Liu-Minipig:
- Stimulation (Team)
- Other: Liu-Minipig: Longitudinal recordings (Team)
- Other: Liu-Minipig: Terminal recording (Team)
- Other: Liu-Minipig: Tongue impression (Team)
- Other: Liu-Minipig: Use of pig sling (Team)
- Other: Liu-Minipig: Baseline recording (Team)
- Other: Liu-Minipig: Catheter and Wire Electrode (Team)
- Other: Liu-Minipig: Pig's training (Team)
- Special Diet: Liu-Minipig: Barium diet (Team)
- Special Diet: Liu-Minipig: Soft diet (Team)
- Special Diet: Liu-Minipig: ad lib feeding with high fat diet (Team)
- Substance
 Administration: Liu-Minipig: Excede

(ceftiofur) injection (Team)

- Substance
 Administration: Liu-Minipig: Post-op analgesic plan (Team)
- Substance
 Administration:
 Analgesia,
 Buprenorphine or
 Buprenorphine SR
 (72 hours)
 (Standard)
- Substance
 Administration: Liu-Minipig:
 Bromodeoxyuridine
 (BrdU)
 Administration
 (Team)
- Substance
 Administration: Liu-Minipig:
 Anesthesia
 Protocol (Team)
- Substance
 Administration: Liu-Minipig:
 Fluorochrome
 Labels for Bone
 (Team)
- Survival
 Surgery: LiuMinipig: Tongue
 base reduction
 surgery (Team)
- Survival
 Surgery: Liu-Minipig:
 Implantation (Team)
- 2. Will any single animal undergo more than one survival surgery? (include any animal that underwent surgery prior to use on this protocol) Yes No
- 3. * Describe the order of and time interval between surgical procedures on a single animal:

For 10 non-obese minipigs in Aim 2. The first survival surgery is the implantation and the second surgery is the coblation - tongue base volume resection surgery. The interval between the two surgeries is at least 10 days.

* Provide scientific justification for multiple survival surgical procedures on a single animal:

The second survival surgery is for investigating the effects of the tongue base volume reduction on respiration and swallowing.

| * | Specify | how ma | any animal | s will | undergo | multiple | survival | surgeries. |
|---|---------|--------|------------|---------|---------|----------|----------|------------|
| | Opecing | | any amma | O AAIII | unucigo | HUHLIPIC | SULAIAGI | Surgeries. |

10 non-obese minipigs for Aim 2

Procedure Personnel Assignment

1. * Select the team members who will be performing each procedure:

| Procedure | Species | Is USDA Species | Team Members |
|---|------------------------------|-----------------------|---|
| Euthanasia: Anesthetic Overdose, Pentobarbital or Pentobarbital Solution, ver. 1 (Standard) | Pigs - Yucatan Minipig | yes | Vet Services |
| Food or Fluid Restriction: Liu- Minipig: Food restriction, ver. 1 (Team) | Pigs - Yucatan Minipig | yes | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu |
| Imaging: Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE), ver. 2 (Team) | Pigs - Yucatan Minipig | yes | Katherine Rafferty Sue Herring Jeffrey Thiel Vet Services Daniel F Leotta Zi-Jun Liu |
| Implants: Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers, ver. 1 (Team) | Pigs - Yucatan Minipig | yes | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu |
| Non-Survival Surgery: Liu-Minipig: Stimulation , ver. 1 (Team) | Pigs - Yucatan Minipig | yes | Katherine Rafferty Sue Herring Vet Services Zi-Jun |

Liu

| Procedure | Is Species USDA Species | Team Members | |
|--|-------------------------------------|---|---------------------------|
| Other: Liu-Minipig: Baseline recording , ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Other: Liu-Minipig: Catheter and Wire Electrode , ver. 3 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | FERPA RCW 42.56.070(1) |
| Other: Liu-Minipig: Longitudinal recordings , ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Other: Liu-Minipig: Longitudinal tracking, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Other: Liu-Minipig: Pig's training, ver 1 (Team) | r. Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |

| Procedure | Is Species USDA Specie | Team Members |
|---|----------------------------------|---|
| Other: Liu-Minipig: Terminal recording , ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu |
| Other: Liu-Minipig: Tongue impression, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu |
| Other: Liu-Minipig: Use of pig sling, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Jeffrey Thiel Vet Services Daniel F Leotta Zi-Jun Liu |
| Special Diet: Liu-Minipig: ad lib feeding with high fat diet, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Jeffrey Thiel Vet Services Daniel F Leotta Zi-Jun Liu |

| Procedure | Is Species USDA Specie | Mamhare | |
|---|----------------------------------|---|---------------------------|
| Special Diet: Liu-Minipig: Barium diet, ver. 2 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | FERPA RCW 42.56.070(1) |
| Special Diet: Liu-Minipig: Soft diet, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services | |
| Substance Administration: Analgesia, Buprenorphine or Buprenorphine SR (72 hours), ver. 2 (Standard) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Jeffrey Thiel Vet Services Daniel F Leotta Zi-Jun Liu | |
| Substance Administration: Liu- Minipig: Anesthesia Protocol, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Vet Services | |
| Substance Administration: Liu- Minipig: Bromodeoxyuridine (BrdU) Administration , ver. 2 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |

| Procedure | Is Species USDA Specie | Team Members s | |
|---|----------------------------------|---|---------------------------|
| Substance Administration: Liu- Minipig: Excede (ceftiofur) injection, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | FERPA RCW 42.56.070(1) |
| Substance Administration: Liu- Minipig: Fluorochrome Labels for Bone, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Substance Administration: Liu- Minipig: Post-op analgesic plan, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Survival Surgery: Liu-Minipig: Implantation, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun Liu | |
| Survival Surgery: Liu-Minipig: Tongue base reduction surgery, ver. 1 (Team) | Pigs - yes Yucatan Minipig | Katherine Rafferty Sue Herring Vet Services Zi-Jun | |

Liu

2. Team member training:

First Name Last Name Training

Sue

| | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | No |
|---------|--|--------------------|--------------|-----------------|-----------------|--------------------|--------------------|----------------------------------|
| | Animal Use Medical Screening | General | Online | Basic Course | Stage 1 | 10/29/2018 | 10/31/2021 | experience data to display |
| | 6th Floor Facility Orientation, Non- Rodent Users | Orientation | In Person | Basic Course | Stage 1 | 10/2/2015 | | |
| | Annual DCM Facility Access Training (Non- Rodent) | General | Online | Basic Course | Stage 1 | 2/27/2020 | 2/28/2021 | |
| | Rabbit Hands-On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 6/26/2012 | | |
| | ARC Facility Orientation, Non- Rodent Users | Orientation | In Person | Basic Course | Stage 1 | 9/27/2017 | | |
| | Surgery Laboratory Part 2 - Waived | Surgery | Other | Basic Course | Stage 1 | 6/22/2016 | | |
| | Pig Hands- On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 10/2/2015 | | |
| | Animal Use Laws & Regulations | General | Online | Basic Course | Stage 1 | 8/3/2017 | 8/3/2022 | |
| | Surgery Laboratory Part 1B - Waived | Surgery | Other | Basic Course | Stage 1 | 6/22/2016 | | |
| Herring | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | No experience |
| | ARC Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | _ | 10/4/2017 | | data to display |
| | Animal Use Laws & Regulations | General | Online | Basic Course | _ | 5/4/2019 | 5/4/2024 | |
| | Mouse Hands-On Laboratory | Animal Handling | In Person | Basic Course | - | 4/22/2014 | | |
| | | | | | | | Obtained b | v Bica for Animala |

| | Course | Category | Source | Stage | Stage Numbe | Completion | on Expiration Date | n |
|--------|---|-------------------------|-----------------------------|---------------------|----------------------------|---------------------------------|---------------------------------|--|
| | Surgery Certification, USDA- Covered Non- Rodents Minor - Waived | Surgery | Other | Basic Course | _ | 1 1/1/1950 | | |
| | Surgery Certification, USDA- Covered Non- Rodents Major - Waived | Surgery | Other | Basic Course | | 1 1/1/1950 | | |
| | Animal Use Medical Screening | General | Online | Basic Course | | 1 10/21/202 | 20 10/31/202 | 23 |
| | Pig Hands- On Laboratory - Waived | Animal Handling | Other | Basic Course | - | 1 1/1/1950 | | |
| | Annual DCM Facility Access Training (Non- Rodent) | General | Online | Basic Course | _ | 1 1/8/2020 | 1/31/202 ⁻ | 1 |
| | Sedation Certification, Rabbit - Waived | Procedure | Other | Basic Course | _ | 1 1/1/1950 | | |
| | Rabbit Hands-On Laboratory | Animal Handling | In Person | Basic Course | | 1 2/24/2011 | | от при |
| | 6th Floor Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | _ | 1 9/24/2004 | 1 | |
| Leotta | Course | Category S | ource S | | tage lumber | Completion Date | Expiration Date | No experience |
| | Animal Use Laws & Regulations | General C | nline B C | asic S ourse | tage 1 | 2/21/2017 | 2/21/2022 | uata to display |
| | Animal Use Medical Screening | General C | nline B | asic S ourse | tage 1 | 6/11/2020 | 6/30/2023 | |
| Leotta | Facility Orientation, Non-Rodent Users Course Animal Use Laws & Regulations Animal Use Medical | Category S General C | Person ource S online B C | tage S asic S ourse | itage lumber itage 1 | Completion Date 2/21/2017 | Expiration Date 2/21/2022 | No experienc data to displa |

Daniel F

| | | Course | Category S | Source S | - | Stage lumber | Completion Date | Expiration Date | |
|--------|-----|--|-----------------------------|--------------|-----------------|-----------------|--------------------|-----------------------|----------------------------------|
| | | Pig Hands- On Laboratory | Animal I Handling I | | | Stage 1 | 4/9/1993 | | |
| Zi-Jun | Liu | Course | Category | Source | Stage | Stage Numbe | Completion | on Expiration Date | No |
| | | 6th Floor Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | | 1 1/7/2014 | | experience data to display |
| | | Regulatory Inspection Training | IACUC Member Training | In Person | Basic Course | | 1 10/28/201 | 15 | |
| | | Animal Use Laws & Regulations | General | Online | Basic Course | _ | 1 8/2/2017 | 8/2/2022 | |
| | | 6th Floor Facility Orientation, Rodent Users | Orientation | | Basic Course | _ | 1 7/5/2005 | | |
| | | Rabbit Hands-On Laboratory | Animal Handling | In Person | Basic Course | | 1 2/24/2011 | | |
| | | Surgery Certification, USDA- Covered Non- Rodents Minor - Waived | Surgery | Other | Basic Course | | 1 1/1/1950 | | |
| | | Surgery Certification, USDA- Covered Non- Rodents Major - Waived | Surgery | Other | Basic Course | | 1 1/1/1950 | | |
| | | Animal Use Medical Screening | General | Online | Basic Course | | 1 7/7/2020 | 7/31/2023 | |
| | | ARC Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | _ | 1 10/4/2017 | 7 | |
| | | T-Wing Facility Orientation | Orientation | | Basic Course | | 1 7/2/2009 | | |

| | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | |
|--------------------|--|--------------------|--------------|-----------------|-----------------|--------------------|--|----------------------------------|
| | Annual DCM Facility Access Training (Rodent) | General | Online | Basic Course | Stage 1 | 5/1/2011 | 5/31/2012 | |
| | Pig Hands- On Laboratory - Waived | Animal Handling | Other | Basic Course | Stage 1 | 1/1/1950 | | |
| | Sedation Certification, Rabbit - Waived | Procedure | Other | Basic Course | Stage 1 | 1/1/1950 | | |
| | Mouse Hands-On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 7/30/2009 | | |
| Katherine Rafferty | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | No |
| | Mouse Hands-On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 5/14/2002 | | experience data to display |
| | Pig Hands- On Laboratory - Waived | Animal Handling | Other | Basic Course | Stage 1 | 1/1/1950 | | |
| | Rabbit Hands-On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 2/24/2011 | оностоят — на она в откат (1007) ПОС откана вина вина вина в | |
| | 6th Floor Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | Stage 1 | 12/22/2015 | | |
| | Surgery Certification, USDA- Covered Non- Rodents Major - Waived | Surgery | Other | Basic Course | Stage 1 | 1/1/1950 | | |
| | Animal Use Laws & Regulations | General | Online | Basic Course | Stage 1 | 7/19/2017 | 7/19/2022 | |
| | Sedation Certification, Rabbit - Waived | Procedure | Other | Basic Course | Stage 1 | 1/1/1950 | | |

| | | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | |
|---------|---|--|--------------------|-----------------|-----------------------------|-----------------|------------------------|--------------------|--------------------|
| | Annual DCM Facility Access Training (Non- Rodent) | General | Online | Basic Course | | 5/7/2019 | 5/31/2020 | | |
| | | Surgery Certification, USDA- Covered Non- Rodents Minor - Waived | Surgery | Other | Basic Course | Stage 1 | 1/1/1950 | | |
| | | ARC Facility Orientation, Non-Rodent Users | Orientation | | Basic Course | Stage 1 | 10/10/2017 | 100 | |
| | | Animal Use Medical Screening | General | Online | Basic Course | Stage 1 | 6/11/2018 | 6/30/2021 | |
| Vet | Services | No training da | ata to display | | | | No expe | erience data | to display |
| Jeffrey | Thiel | Course | Category | Source | Stage | Stage Number | Completion Date | Expiration Date | No experience |
| | | Pig Hands- On Laboratory | Animal Handling | In Person | Basic Course | Stage 1 | 1/29/2019 | | data to display |
| | | , | | | | | | | WW. |
| | | Animal Use Medical Screening | General | Online | Basic Course | Stage 1 | 2/21/2019 | 2/28/2022 | |
| | | Animal Use Medical | General General | Online | Course | | 2/21/2019 1/18/2020 | | |
| | | Animal Use Medical Screening Annual DCM Facility Access Training (Non- | | Online | Course Basic Course Basic | Stage 1 | | | |

| Course | Category | Source | Stage | Stage Number | Completion Date | Date |
|---|-------------|--------|--------|-----------------|--------------------|------|
| WaNPRC Surgery Suite Clearance | Orientation | | Course | J | 1/19/2017 | |
| Animal Use Laws & Regulations | | Online | | | 3/10/2016 | |

Animal Details

* How are animals acquired?

2. Describe the acquisition for:

a. Not purchasing through DCM or WaNPRC: N/A

- 3. Identification of individual animals (other than cage cards):
 - a. Method(s) (e.g., ear punch/tag, tattoo, tagging/banding, radio collar, etc.) (Note: If method is implantation (e.g. PIT tag), create or select an Implant procedure to describe the details. If method is surgical (e.g., satellite tag), create or select Survival Surgery procedure to describe the details):
 N/A
 - **b.** Will external identification be replaced if it falls off/out? If yes, describe the plan for replacement:

N/A

- C. Will external identification be removed as part of the protocol (e.g., radio collars on field animals)? If yes, describe the plan for removal:
 N/A
- 4. Identify strain/stock for rodents and genetically modified animals:

Species Is USDA Species Strain Genetically Modified Strain Phenotype Description There are no items to display

Animal Number Adjustments

"Animals Identified in Experiments" is the total number of animals per pain category listed in all experiments on this protocol. If more or fewer animals will be used on the protocol (see Help Text for examples), click Update to enter this new number in the corresponding "Adjusted Animal Count" column. **Only input numeric values in this field; 0 is acceptable.**
If no adjustment is required, the values in the "Animals Identified in Experiments" and "Adjusted Animal Count" columns must match. Click Update in each Pain Category row to input the matching value.

For questions about adjusting animal numbers, contact OAW.

1. * Click Update to adjust the number of animals to be used or produced for this protocol:

| | Species | USDA Covered Species | Pain Category | Animals Identified in Experiments | Adjusted Animal Count |
|------|------------------------------|----------------------------|-----------------------|---|-----------------------------|
| View | Pigs - Yucatan Minipig | yes | Pain Category B | 0 | 0 |
| View | Pigs - Yucatan Minipig | yes | Pain Category C | 0 | 0 |
| View | Pigs - Yucatan Minipig | yes | Pain Category D | 30 | 30 |
| View | Pigs - Yucatan Minipig | yes | Pain Category E | 0 | 0 |

- 2. If you adjusted the number of animals for this protocol, explain why:
- 3. If you will be using animals to train personnel or to practice procedures included in this protocol, describe below:

 N/A
- 4. Supporting documents:

Document Name Date Modified

There are no items to display

Alternatives and Duplication Searches

Display Procedures that cause pain or distress:

- Other: Liu-Minipig: Baseline recording, ver. 1 (Team)
- Other: Liu-Minipig: Catheter and Wire Electrode, ver. 3 (Team)
- Survival Surgery: Liu-Minipig: Implantation, ver. 1 (Team)
- Other: Liu-Minipig: Longitudinal recordings, ver. 1 (Team)
- Other: Liu-Minipig: Longitudinal tracking, ver. 1 (Team)
- Implants: Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers, ver. 1 (Team)
- Non-Survival Surgery: Liu-Minipig: Stimulation, ver. 1 (Team)
- Other: Liu-Minipig: Terminal recording, ver. 1 (Team)
- Survival Surgery: Liu-Minipig: Tongue base reduction surgery, ver. 1 (Team)
 - 1. Record all searches for any previous research that this protocol might duplicate:

| Search Date | Searched Databases | Other |
|----------------|---|-------|
| View 7/3/2020 | Web of Science (searches multiple databases) PubMed/Medline | N/A |

2. Briefly describe the results of your searches and why you can or cannot incorporate the findings. Or, if a literature search was not performed, describe the methods used to determine that alternatives are not available or feasible:

Based on this literature search, the minipigs is proven to be the best non-primate model for study of oropharyngeal function and malfunction to date, because its similarity to humans in oropharyngeal apparatus and its appropriate size for necessary instrumentation for examining these physiological and phthophysiological characters.

3. Confirm that you have made every effort to ensure that this protocol is not unnecessary duplication of previous research: ✓

View: Custom SF: Housing and Use

Housing and Use

Housing and use outside of the vivarium is not allowed without strong scientific justification.

1. Identify each location where animals will be housed:

| | Facility | Species | Justification for Housing Outside Vivarium |
|------|------------------|---------------------------|---|
| View | Brotman ABSL1 | Pigs - Yucatan Minipig | N/A |
| View | ARCF ABSL1 | Pigs - Yucatan Minipig | Housing relocation for all USDA large animals |

2. Identify each location where animals will be used:

| | Facility | Use | Species | Justification for Use Outside Vivarium |
|------|------------------|--|---------------------------|---|
| View | | All surgical procedures and recording sessions | Pigs - Yucatan Minipig | N/A |
| View | Brotman ABSL1 | MRI | Pigs - Yucatan Minipig | N/A |

View: Custom SF: Disposition

Disposition

1. Disposition plans for the animals when this research is complete:

(check all that apply) Euthanasia

2. If other, provide an animal disposition description:

N/A

3. If protocol involves fixing tissues, list agents (e.g., paraformaldehyde, formalin):

Paraformaldehyde, and microfil (casting of tongue vasculature)

Refinement, Replacement and Reduction

- 1. Describe below how the three R's (refinement, replacement and reduction) have been employed on this project. Include alternatives that were considered for the procedures above that cause pain or distress:
 - * Refinement (use of methods to decrease animals' sensitivity to pain)

Potentially painful procedures are always mitigated with analgesics, or the animals are fully sedated.

- * Replacement (include in vitro tests, use of less sentient animals)
 It is not possible to use a less sentient animal in this type of study without compromising the relevance to human physiology and function.
- * Reduction (use of fewer animals to attain statistical significance) We have utilized a power analysis to determine the least number of pigs needed to complete these studies and achieve significance.
- 2. Describe the rationale for using animals and the appropriateness of the species proposed:

This project is to study the tongue base function, malfunction, and regeneration, Pigs are chosen because of their similarity to the human in the oral structure and upper airway among non-primate species in both morphological and functional aspects, and their large sizes are adequate for necessary instrumentation for functional recording of oropharynx.

Supporting Documents

1. Attach supporting files:

Document Name Date Modified

Liu_3393-05_Portfolio.pdf 7/3/2020 2:00 PM

Procedures Appendix:



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Pig's training

1. * Name of the procedure or surgery:

Liu-Minipig: Pig's training

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

View: Custom SF: Other

Other

1. Description of Procedure:

The pig will be trained to walk up to the feed table and to feed on the table. This is a routine procedure in Sue Herring's and my lab for all pig projects. The table is used to restrain the pig during feeding and allows the x-ray tube to be placed underneath the pig's body. During feeding, the pig jacket will be placed on the pig's back but it will not be wearing the jacket. This is to prepare the pig to have a jacket on when it wakes up from anesthesia during the recording session.

The pig will be trained to get used to the pig sling. During the training, the pig will be placed in the pig sling for feeding.

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Longitudinal tracking

1. * Name of the procedure or surgery:

Liu-Minipig: Longitudinal tracking

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- **i.** Identify expected symptoms from administering this procedure: The pig may struggle to get rid of recording devices connected.
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Other

Other

1. Description of Procedure:

During each recording session, under anesthesia, the skin button and EMG micro connectors will be connected to the relevant devices. The longitudinal recordings include tongue base 3D deformation (distance changes between each SONO crystal pair), respiratory dynamics (videofluoroscopic images) and parameters (facemask and nasal catheter connecting to the Pneumotach and BioRadio systems, respectively), and muscular activity (EMG). Recording from these devices will simultaneously be carried out for 10-15 minutes either when the pig is under light anesthesia or during unrestrained feeding of barium diet.

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Use of pig sling

1. * Name of the procedure or surgery:

Liu-Minipig: Use of pig sling

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

View: Custom SF: Other

Other

1. Description of Procedure:

A pig sling may be used during each recording session as the Vet Services recommended.

Pig sling training is included in the training session.

After the instrumentation under sedation, the pig will be placed in the pig sling for all recordings including: baseline, longitudinal. pre-surgical, and terminal recordings.

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Longitudinal recordings

1. * Name of the procedure or surgery:

Liu-Minipig: Longitudinal recordings

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- **i.** Identify expected symptoms from administering this procedure: The pig may struggle to get rid of recording devices connected.
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Other

Other

1. Description of Procedure:

During each recording session, under anesthesia, the skin button and EMG micro connectors will be connected to the relevant devices. The longitudinal recordings include tongue base 3D deformation (distance changes between each SONO crystal pair), respiratory dynamics (videofluoroscopic images) and parameters (facemask and nasal catheter connecting to the Pneumotach and BioRadio systems, respectively), and muscular activity (EMG). Recording from these devices will simultaneously be carried out for 10-15 minutes either when the pig is under light anesthesia or during unrestrained feeding of barium diet.

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers

1. * Name of the procedure or surgery:

Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers

2. * Select procedure type:

Implants

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

i. Identify expected symptoms from administering this procedure:

Pain, swelling and possible infection around the incisions.

ii. Identify criteria under which animals will be removed from research:

Uncontrolled infection or > 20% loss of body weight.

View: Custom SF: Implants

Implants

1. Type, including approximate size and weight:

8 SONO crystals: 2mm in diameter, 0.05g

8 pairs of wire EMG electrodes: 0.10mm in diameter, 0.01g.

4 metal balls with barbs: 1mm in diameter, 0.8g 2 metal balls without barbs: 1mm in diameter, 0.7g

3 stainless steel miniscrews: 1mm in size, 0.3g.

1 skin button for SONO recording: 20mm in size, 20g.

1 EMG microconnector: 15mm in size, 10g

2. Site:

Tongue base (crystals; pharyngeal muscles (EMG electrodes); soft palate, hyoid, and thyroid cartilage (metal balls); and alveolar bones (miniscrews),; skin button ans microconnector: pig's back.

3. Maintenance and care of chronic implants:

Skin button and micro-connector will be checked and iodine solution will be used to clean the incisions and skin button/micro-connector area for the first 5-7 days after the implantation. Antibiotic ointment or powder will be used per Vet Services' recommendation. After the first week, this check up will be three times a week.

The implanted crystals, wire EMG electrodes, metal balls and miniscrews will be checked during each recording session.

4. Method used to sterilize implants:

Autoclave

5. Describe implant procedure (if the implant is surgical, create a new Survival Surgery procedure and refer to it here):

Please refer to the implantation surgery.

6. Monitoring protocol:

Twice a day for 5-7 days after the implantation, then check during each session of recording.

7. Will it be necessary to surgically remove implants, or to re-implant or repair implants if they fail? If so, describe the circumstances and the maximum number of replacements if applicable:

No removing implants.

If some SONO crystals fail, we may re-implant them only during the terminal recording, and the number will be limited to less than 4 crystals. This re-implanting will be via a submandibular approach, as for the implantation surgery. Since the animal will be euthanized after the terminal recording, this re-implanting is not considered as chronic implants.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Stimulation

1. * Name of the procedure or surgery:

Liu-Minipig: Stimulation

2. * Select procedure type:

Non-Survival Surgery

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure:

 None, as all procedures will be performed under anesthesia.
- ii. Identify criteria under which animals will be removed from research: N/A

Non-Survival Surgery

* Describe how the animal, surgeon, and instruments will be prepared for surgery:

This is a non-survival procedure. No sterilized instruments will be required but instruments will be clean.

The pigs will be fasted overnight. Water will be available.

Surgeon will wear lab coat or surgical scrubs, mask and gloves, and the animal will be prepared by cleaning their skin in the area of the surgical site. Hair will be removed if necessary.

2. * Describe the surgical procedure:

After the terminal recording, the pig will be re-anesthetized, placed supine, and the bilateral hypoglossal nerve complex, including nerve trunk (HG), and its medial (HGM) and lateral (HGL) branches, genioglossus (GG), and stylogossus (SG) will be exposed and isolated through a submandibular approach. For nerve stimulation, custom-made silver bipolar cover-tube electrodes will be placed around the dissected bilateral HGs, HGMs and HGLs (3-5 mm caudal or rostral to the nerve furcation, respectively. The proximal nerve stumps will be cauterized and mineral oil will be used to cover the exposed nerves to prevent current spread. For muscle stimulations, 0.1mm-thick bipolar wire electrodes will be directly inserted into the bellies of targeted muscles at an interpolar distance of 10mm. The stimulation electrodes will be connected to a stimulation isolation unit and the stimulator will be set up: 1) Nerves: 600ms trains, 0.5ms pulse, and 3-15V intensity, 2) Muscles: 600ms trains, 5ms pulse, and 10-40V intensity. The voltage will be ramped up to the titanic level, determined by plateauing at the deformations of tongue base or soft palate and peak airflow pressure. 3D deformational changes in the tongue base (SONO) and respiratory parameters (Pneumotach system) will be recorded along with stimulation pulses under x-ray videofluoroscopy. This stimulation will be performed under anesthesia for about 20-30 minutes. The entire stimulation session will last about 50-60 minutes.

After the completion of the stimulation session, the pig will be euthanized with pentobarbital.

3. * Select associated substance administration procedures, including anesthesia and analgesia procedures to be used:

Liu-Minipig: Anesthesia Protocol

Substance Administration

1 Team

4. Describe how animals will be monitored during the procedure, including anesthetic monitoring:

Anesthetic monitoring by Vet Services

5. Describe how death will be confirmed:

No heart beetling.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Baseline recording

1. * Name of the procedure or surgery:

Liu-Minipig: Baseline recording

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- **i.** Identify expected symptoms from administering this procedure: The pig may struggle to get rid of recording devices connected.
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Other

Other

1. Description of Procedure:

Under light anesthesia, a pair of wire electrodes (0.1mm) will be inserted into the right middle pharyngeal constrictor muscle and the placement of a face mask connecting with pneumotach sensor. After a few minutes, the following will take place: recording of x-ray videofluoroscopy, replacement of the face mask by a French red rubber catheter inserted into the right nasal cavity 3-5cm deep and secured to nearby nasal skin by suturing, and placements of chest/abdominal belts and oximeter ear clip. The red rubber catheter is for recording the respiratory parameters via BioRadio system

during feeding. The catheter, EMG leads, belts, and oximeter will be connected to a BioRadio receiver box in the back pocket of the jacket.

After waking up, the videofluoroscopic swallowing examination (VFSE) will be performed for respiration and voluntary swallowing during unrestrained feeding. After 10-15 minutes of feeding on the barium diet, catheter, sensors and wire electrodes, as well as the jacket will be removed, and the pig will be returned to its pen.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Anesthesia Protocol

1. * Name of the procedure or surgery:

Liu-Minipig: Anesthesia Protocol

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration | Volume | Substance Order for the Procedure |
|------|---|--------------------|-------|-------------------|---------------|--------|--|
| View | Vet Services Administered Anesthetics | | Other | See attachment | N/A | N/A | N/A |

2. * Describe step-by-step the procedure for administering the substance(s):

Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended.

3. Describe the intended effects of administering the substance(s):

Anesthesia

4. Describe any potential adverse reactions to administering the substance(s):

Some anesthetic agents may have adverse effects, such as causing hyperthermia during anesthesia or ataxic behavior during recovery. Such effects vary with the agent used. For specific agents, please check with veterinary staff.

5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.

Anesthetic gases such as isoflurane are hazardous with chronic exposure and therefore we scavenge them with f/air canisters.

6. * Does this procedure include the use of a paralytic agent?

Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

1. Supporting documents:

| Document Name | Date Modified |
|--|-----------------------|
| Vet Services Administered Anesthetics- Agent, Rout, Dosage.PNG | 11/23/2016 5:40 PM |

1. * Substance:

Vet Services Administered Anesthetics

2. Route:

Other

If you indicated Other, specify the route:

Multiple

3. Dose:

See attachment

4. Frequency and duration of dosages:

See attachment

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Pharmaceutical grade

8. Complication remediation:

Respiration is monitored using a pneumotach. Heart rate and temperature will be checked manually. Corneal reflex and toe pinch will be used to monitor anesthesia depth.

9. Substance order for the procedure:

N/A



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Catheter and Wire Electrode

1. * Name of the procedure or surgery:

Liu-Minipig: Catheter and Wire Electrode

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

i. Identify expected symptoms from administering this procedure:

Procedure will be done under light anesthesia, and the catheter and wire EMG electrodes will be removed after the baseline recording.

The catheter will be sutured to the nearby skin around the nose. After recording, the suture will be removed without anesthesia as did for the previous live sleep monitoring in minipigs.

ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Other

Other

1. Description of Procedure:

Under light anesthesia, insertion of a pair of wire electrodes (0.1mm) into the right middle pharyngeal constrictor muscle and the placement of a face mask connecting with pneumotach sensor. After a few minutes recording of x-ray videofluoroscopy, replacement of the face mask by a #10 French red rubber catheter inserted into the right nasal cavity 3-5cm deep and secured to nearby nasal skin by suturing, and placements of chest/abdominal belts and oximeter ear clip. Catheter, EMG leads, belts, and oximeter will be connected to a BioRadio receiver box in the back pocket of the jacket. After waking up, the videofluoroscopic swallowing examination (VFSE) will be performed for respiration and voluntary swallowing during unrestrained feeding. After 10-15' of feeding on the barium diet, sensors wire electrodes, and catheter will be removed without further anesthesia, and the pig will return to its pen. The procedures of these removal will be the same as we did in live sleep monitoring in minipigs.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Bromodeoxyuridine (BrdU) Administration

1. * Name of the procedure or surgery:

Liu-Minipig: Bromodeoxyuridine (BrdU) Administration

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration | Volume | Substance Order for the Procedure |
|------|---|--------------------|--------------------------|-------------|---------------|--------|--|
| View | Saline | Standard | Intravenous - Various | 10 mg/ml | N/A | N/A | W/BrdU |
| View | 5- Bromodeoxyuridine (BrdU, 5-bromo- 2'deoxyuridine) | | Intravenous - Various | 40mg/Kg | N/A | N/A | w/Saline |

2. * Describe step-by-step the procedure for administering the substance(s):

Pig will be IV injected per the above doses.

The first injection will be performed during the week 3 longitudinal recording, and the second injection will be performed during the last tongue impression, MRI and EUS. So, no additional anesthetic session is needed for these injections.

3. Describe the intended effects of administering the substance(s):

Label dividing cells. No anticipated side effects.

4. Describe any potential adverse reactions to administering the substance(s):

None expected

5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.

Potential danger to humans: Mutagen

Precautions to protect personnel: gloves, lab coat, face mask

Special containment requirements: None required

Special disposal requirements for agents and animals: None required

6. * Does this procedure include the use of a paralytic agent?

Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

View: SF: Procedure Documents

Procedure Documents

1. Supporting documents:

Document Name Date Modified

There are no items to display

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|---|-----|----|----|-----|----|---|----|
| | | | | | | | |

Saline

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

10 mg/ml

4. Frequency and duration of dosages:

Up to twice w/BrdU

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Saline is pharmaceutical grade.

8. Complication remediation:

N/A

9. Substance order for the procedure:

W/BrdU

1. * Substance:

5-Bromodeoxyuridine (BrdU, 5-bromo-2'deoxyuridine)

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

40mg/Kg

4. Frequency and duration of dosages:

Up to twice

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Agent is not available in pharmaceutical grade. It will be diluted in pharmaceutical grade saline.

8. Complication remediation:

Check daily. Animals should be alert, active and hungry

9. Substance order for the procedure:

w/Saline



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: ad lib feeding with high fat diet

1. * Name of the procedure or surgery:

Liu-Minipig: ad lib feeding with high fat diet

2. * Select procedure type:

Special Diet

3. * Species:

Pigs - Yucatan Minipig

| i. Identify expected symp | toms from administ | ering this procedu | ıre: | |
|-------------------------------|---------------------|--------------------|---------|--|
| ii. Identify criteria under w | hich animals will b | e removed from re | search: | |
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4. * Will administering this procedure cause any more than momentary

pain or distress? Yes No

Special Diet

1. Composition of Diet:

High fat diet will be provided by the minipig vendor, S&S Farms.

2. Amount:

ad lib

3. Duration:

During the entire experimental period for obese minipigs only.

4. Rodents only: verify that foods/treats (except sucrose pellets) will be autoclaved or irradiated:

Yes

No

If No, provide justification here (Note: cost is not sufficient justification):

5. Intended effects on animals:

Gain weight.

6. Potential side-effects on animals:

None expected.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Barium diet

1. * Name of the procedure or surgery:

Liu-Minipig: Barium diet

2. * Select procedure type:

Special Diet

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Special Diet

Special Diet

1. Composition of Diet:

50 ml of 22% barium suspension will be mixed with 500g regular pig pellets.

2. Amount:

500g

3. Duration:

During each recording session, about 15-20 minutes.

4. Rodents only: verify that foods/treats (except sucrose pellets) will be autoclaved or irradiated:

Yes

No

If No, provide justification here (Note: cost is not sufficient justification):

This is a routine procedure in humans for examining swallowing function under x-ray fluoroscopy

5. Intended effects on animals:

Outlining the dynamic imagings of oropharyngeal structures during swallowing.

6. Potential side-effects on animals:

None

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Tongue impression

1. * Name of the procedure or surgery:

Liu-Minipig: Tongue impression

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

View: Custom SF: Other

Other

1. Description of Procedure:

Under anesthesia, the mouth will be opened widely by the two mouth openers. A customized tray filled with impression material (Alginate) will be inserted into the mouth to cover entire tongue. After 2-3 minutes (Alginate setting), the tray will be taken out with the tongue impression.

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE)

1. * Name of the procedure or surgery:

Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE)

2. * Select procedure type:

Imaging

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Imaging

Imaging

1. Imaging types:

Elastography (e.g., Tactile Imaging)
Magnetic Resonance Imaging (e.g., MRI, fMRI)
Other
Ultrasonography (Ultrasound)

2. If Other, specify:

videofluoroscopic swallowing examination (VFSE)

3. Select the anesthesia and analgesia procedures to be used:

Liu-Minipig: Vet Services Administered Anesthestics Substance Administration 2 Team

4. Frequency, including minimum time between imaging sessions and the maximum number of sessions (enter specific, detailed procedure timing in the Experiment):

MRI and Ultrasound: twice; VFSE: 6 times

5. Duration of imaging session:

30 min for MRI, 5-10 min for Ultrasound, and 15-20 min for SVF

6. Purpose:

Imaging and videofluoroscopic swallowing examination (VFSE)

7. Will supportive care of animals be necessary during the imaging session?

Yes No

8. If yes, describe:

N/A

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Post-op analgesic plan

1. * Name of the procedure or surgery:

Liu-Minipig: Post-op analgesic plan

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration Volume | Substance Order for the Procedure |
|------|-------------------------|--------------------|--------------------------|---|----------------------|---|
| View | Fentanyl (Sublimaze) | Standard | Transdermal | vet services will determine correct patch size/dose | | |
| View | Carprofen (Rimadyl) | Standard | Subcutaneous | 2-4 mg/kg | | Only one Carprofen route will be used. |
| View | Carprofen (Rimadyl) | Standard | Intravenous - Various | 2-4 mg/kg | | Only one Carprofen route will be used. |
| View | Carprofen (Rimadyl) | Standard | Oral - Other | 2 mg/kg | | Only one Carprofen route will be used. |

2. * Describe step-by-step the procedure for administering the substance(s):

72 hr of opioid (one dose of SR buprenorphine or multiple doses of regular buprenorphine or fentanyl patch) and 72 hr of NSAID (e.g., carprofen 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr).

- **3.** Describe the intended effects of administering the substance(s): Pain relief.
- 4. Describe any potential adverse reactions to administering the substance(s):

Vet Services will monitor these

- 5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.
- 6. * Does this procedure include the use of a paralytic agent?

 Yes No

| aperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu. | | | | | | | | |
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View: SF: Procedure Documents

Procedure Documents

1. Supporting documents:

Document Name Date Modified

There are no items to display

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Fentanyl (Sublimaze)

2. Route:

Transdermal

If you indicated Other, specify the route:

3. Dose:

vet services will determine correct patch size/dose

4. Frequency and duration of dosages:

one patch, lasts 72 hr

- 5. Volume (for rodents or intracranial injections):
- 6. Concentration:
- 7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Fentanyl will be pharmaceutical grade.

- 8. Complication remediation:
- 9. Substance order for the procedure:

| 1 | _ | * | S | П | bs | sta | ın | C | e | |
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Carprofen (Rimadyl)

2. Route:

Subcutaneous

If you indicated Other, specify the route:

3. Dose:

2-4 mg/kg

4. Frequency and duration of dosages:

Every 24 hr for up to 72 hr

- 5. Volume (for rodents or intracranial injections):
- 6. Concentration:
- 7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Carprofen will be pharmaceutical grade.

8. Complication remediation:

None expected.

9. Substance order for the procedure:

Only one Carprofen route will be used.

1. * Substance:

Carprofen (Rimadyl)

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

2-4 mg/kg

4. Frequency and duration of dosages:

every 24 hr

- 5. Volume (for rodents or intracranial injections):
- 6. Concentration:
- 7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Carprofen will be pharmaceutical grade.

8. Complication remediation:

None expected.

9. Substance order for the procedure:

Only one Carprofen route will be used.

1. * Substance:

Carprofen (Rimadyl)

2. Route:

Oral - Other

If you indicated Other, specify the route:

3. Dose:

2 mg/kg

4. Frequency and duration of dosages:

Every 12 hr up to 72 hrs

- 5. Volume (for rodents or intracranial injections):
- 6. Concentration:
- 7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Carprofen will be pharmaceutical grade.

8. Complication remediation:

None expected

9. Substance order for the procedure:

Only one Carprofen route will be used.



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Food restriction

1. * Name of the procedure or surgery:

Liu-Minipig: Food restriction

2. * Select procedure type:

Food or Fluid Restriction

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

| N/A | | | |
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i. Identify expected symptoms from administering this procedure:

ii. Identify criteria under which animals will be removed from research:

N/A

Food or Fluid Restriction

1. * Restrictions:

Food

2. * Provide the maximum number of hours food/fluid will be restricted:

24

3. * Describe the procedure for providing food/fluid including schedules and amounts:

Only food is restricted, (just the timing of the feeding, not calories), 12-16 hours before each session of training and anesthesia for the surgeries and recordings. No more than 24 hr will elapse between feedings.

4. * Describe criteria for monitoring the health of animals while on food/fluid restriction:

Animals will be monitored for food and water intake following fasting and anesthetic events. Body weight will be monitored once a week.

5. * Provide justification for restricting food/fluid to the extent defined:

Necessary for general anesthesia, and good for training on the feeding table for living fluoroscopy.

6. Describe what will happen if animals fail to meet selected health criteria:

No side effects are expected. Animals will be fed a normal ration (i.e., calories will not be limited).

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Anesthetic Overdose, Pentobarbital or Pentobarbital Solution

1. * Name of the procedure or surgery:

Anesthetic Overdose, Pentobarbital or Pentobarbital Solution

2. * Select procedure type:

Euthanasia

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

View: Custom SF: Euthanasia

Euthanasia

1. * Method of euthanasia:

Anesthetic Overdose

2. Describe procedure:

Pigs will be injected IV with pentobarbital (Nembutal) or a pentobarbital solution at a dose of at least 87 mg/kg.

Examples of pentobarbital solutions include Beuthanasia, Euthasol and similar solutions containing a mixture of pentobarbital and phenytoin. Dosing is based on the pentobarbital component of the solution.

- 3. * Will anesthesia be used? Yes No
- 4. Describe how death will be confirmed:

Death will be confirmed by lack of respirations and heartbeat.

5. Is this method approved by the AVMA Guidelines on Euthanasia (2013)?

Yes No

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Fluorochrome Labels for Bone

1. * Name of the procedure or surgery:

Liu-Minipig: Fluorochrome Labels for Bone

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure: N/A
- ii. Identify criteria under which animals will be removed from research: N/A

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration | Volume | Substance Order for the Procedure |
|------|-------------------------|--------------------|--------------------------|---------------|---------------|--------|---|
| View | Saline | Standard | Intravenous - Various | 5mg/ml | N/A | N/A | w/flurochromes |
| View | Alizarine Complexone | Team | Intravenous - Various | 12.5 mg/kg | N/A | N/A | w/Saline |
| View | Calcein | Team | Intravenous - Various | 12.5 mg/kg | N/A | N/A | w/Saline |

2. * Describe step-by-step the procedure for administering the substance(s):

Bone labels, calcein and alizarine complexone, will be administered through IV (ear vein) at the following dose: 12.5mg/kg in a 5mg/ml sterile saline solution, pH adjusted.

Alizarine injection will be performed on the day of the last tongue impression, MRI and EUS, but the calcein injection will need an additional anesthetic session on 7 days before the terminal recording.

- 3. Describe the intended effects of administering the substance(s): labels mineralizing bone
- **4.** Describe any potential adverse reactions to administering the substance(s):

No anticipated side effects

- 5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.
- 6. * Does this procedure include the use of a paralytic agent?

 Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

View: SF: Procedure Documents

Procedure Documents

1. Supporting documents:

Document Name Date Modified

There are no items to display

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| | | | | | | | | |

Saline

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

5mg/ml

4. Frequency and duration of dosages:

Twice, mixed with Calcine and Alizarin 7 and 2 days before the terminal day

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

N/A

8. Complication remediation:

Check daily. Animals should be alert, active and hungry

9. Substance order for the procedure:

w/flurochromes

1. * Substance:

Alizarine Complexone

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

12.5 mg/kg

4. Frequency and duration of dosages:

Once, 2 days before the terminal day.

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Not available in pharmaceutical grade. We will use a .22 micron filtered syringe when injecting.

8. Complication remediation:

Check daily. Animals should be alert, active and hungry

9. Substance order for the procedure:

w/Saline

1. * Substance:

Calcein

2. Route:

Intravenous - Various

If you indicated Other, specify the route:

3. Dose:

12.5 mg/kg

4. Frequency and duration of dosages:

Once, 7 days before the terminal day.

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Not available in pharmaceutical grade. We will use a .22 micron filtered syringe when injecting.

8. Complication remediation:

Check daily. Animals should be alert, active and hungry

9. Substance order for the procedure:

w/Saline



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Terminal recording

1. * Name of the procedure or surgery:

Liu-Minipig: Terminal recording

2. * Select procedure type:

Other

3. * Species:

Pigs - Yucatan Minipig

| 4. * Will administering | ng this | procedure | cause | any i | more | than | moment | ary |
|-------------------------|---------------|-----------|-------|-------|------|------|--------|-----|
| pain or distress? | Yes No | | | | | | | |

If yes,

- **i.** Identify expected symptoms from administering this procedure: The pig may struggle to get rid of recording devices connected.
- ii. Identify criteria under which animals will be removed from research: $\ensuremath{\mathsf{N/\!A}}$

View: Custom SF: Other

Other

1. Description of Procedure:

Two days before the terminal recording, tongue impression, MRI and ultrasound elastography (EUS) will be performed.

On the terminal day, there will be a terminal recording, which is the same as the recordings during longitudinal tracking. The animals are first anesthetized to connect the instrumentation (takes 10-15 min) and the animals then wake up for the recording session.

After terminal recording, the stimulation session will be performed. this is a non-survival procedure (see stimulation).

Procedure Documents

1. Supporting documents:

Document Name

Date Modified

There are no items to display



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Excede (ceftiofur) injection

1. * Name of the procedure or surgery:

Liu-Minipig: Excede (ceftiofur) injection

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

Cubatanaa

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration Volume | Order for the Procedure |
|------|---|--------------------|---------------|--------------|----------------------|-------------------------------|
| View | Ceftiofur sodium (Naxcel, Ceftiflex) | Standard | Intramuscular | 2- 5mg/Kg | 200 mg/ml | |

2. * Describe step-by-step the procedure for administering the substance(s):

Injection of Excede (ceftiofur) at the time of implantation and tongue base volume reduction surgeries. . One injection at the time of surgery lasts for approx. 5 days.

- **3.** Describe the intended effects of administering the substance(s): Prophylactic infection control.
- **4.** Describe any potential adverse reactions to administering the substance(s):

None

- 5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.
- 6. * Does this procedure include the use of a paralytic agent?

 Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

View: SF: Procedure Documents

Procedure Documents

1. Supporting documents:

Document Name Date Modified

There are no items to display

1. * Substance:

Ceftiofur sodium (Naxcel, Ceftiflex)

2. Route:

Intramuscular

If you indicated Other, specify the route:

3. Dose:

2-5mg/Kg

4. Frequency and duration of dosages:

once

- 5. Volume (for rodents or intracranial injections):
- 6. Concentration:

200 mg/ml

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

will be pharmaceutical grade

8. Complication remediation:

None

9. Substance order for the procedure:



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Tongue base reduction surgery

1. * Name of the procedure or surgery:

Liu-Minipig: Tongue base reduction surgery

2. * Select procedure type:

Survival Surgery

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

i. Identify expected symptoms from administering this procedure:

Pain, and possible infection, and damage on tongue function during feeding.

For pain relief and infection control, pigs will be given an opioid for a minimum of 72 hr (either a Fentanyl patch, SR buprenorphine, or regular buprenorphine) and the NSAID Carprofen for a minimum of 72 hr.

Soft diet will be offered after the surgery.

ii. Identify criteria under which animals will be removed from research:

Severe infection and >20% loss of body weight

Survival Surgery

1. * Surgery Type:

Maior

2. * Describe how the animal, surgeon, and instruments will be prepared for surgery:

Only non-obese minipigs in Aim 2 will have this surgery. The PI and his lab staff will be the surgeon or assistant. The surgery will be performed in the surgical center of the animal facility with on site Vet support.

Instruments will be sterilized by autoclave.

Animal: Animals will be fasted minimum of 12 hours before surgery. Water will be available at all times. Skin incision site(s) will be clipped of any hair, scrubbed with betadine/ chlorhexidine soap and wiped clean with alcohol for a minimum of 3 alternating wipes.

Surgeon: Surgical gown, mask and sterile surgical gloves will be worn.

3. * Describe the surgical procedure, including any deficits expected as a result of the surgery:

The tongue base volume reduction surgery will be performed for non-obese minipigs only (n=10). There will be no surgical intervention in the obese sibling. A dose of Excede (antibiotics) will be administered IM a t the start of the surgery. The surgical region will be the center area surrounded by 8 implanted SONO crystals by the implantation surgery. This surgery is called coblation. Coblation uses the principle of electro-dissociation. removing tissue by means of low-temperature ionization at 100-160°C with simultaneous saline irrigation, in contrast to conventional electrosurgery at 400-600°C. Therefore, coblation should theoretically produce less collateral tissue damage, fewer postoperative complications, and faster wound healing than full-invasive electrosurgery, and be more effective in volume reduction.

Under anesthesia, the procedure will begin by creating a 20mm midline incision at the location 20mm posterior to the circumvallate papillae. The wand tip will diverge to meet the lateral margin anteriorly and to remove two triangular wedges. To create a uniform defect, the lesion will be within the SONO crystal circumscribed zone with 20mm length, 15mm width, and 10mm depth. The lesion will be closed with absorbable sutures in 2-3 layers (See Fig. 3: Coblation).

Coblation will then be applied to one (decided by coin toss) masseter muscle (MA), Skin incision (1.5cm) site will be clipped of any hair, scrubbed with betadine/ chlorhexidine soap and wiped clean with alcohol for a minimum of 3 alternating wipes. The coblation will be applied in the exposed MA with the size of 5x5x5mm.

Synthetic absorbable suture will be used for any internal (e.g., muscle, SC) layers requiring closure. Synthetic non-absorbable suture will be used for skin closure. Skin sutures will be removed by 14 days post-op, generally during a planned anesthetic event (e.g., tracking)

Immediately after the coblation, SONO measurements will be taken and the actual volumetric decrease will be calculated using SonoVol. The entire surgery will take 1 to 1.5 hours.

The deficits of this survival surgery include pain and swollen around the surgical area. bases on our experience from previous tongue body volume reduction surgery, these

deficits will last 5-7 days. In addition, eating will be affected due to the pain and swollen. Soft food will be provided after the surgery for 7 days.

4. * Select associated substance administration procedures, including anesthesia and analgesia procedures to be used:

| Analgesia, Buprenorphine or Buprenorphine SR (72 hours) | Substance Administration | 2 Standard |
|---|-----------------------------|------------|
| Liu-Minipig: Anesthesia Protocol | Substance Administration | 1 Team |
| Liu-Minipig: Excede (ceftiofur) injection | Substance Administration | 1 Team |
| Liu-Minipig: Post-op analgesic plan | Substance Administration | 1 Team |

5. Describe how animals will be monitored during the procedure:

The animal is under anesthesia during the procedure and will be monitored by the staff of Vet Services. Vet services will monitor HR, body temperature, respiratory rate, blood pressure, and oxygen saturation.

6. Describe the routine for postoperative care: (including removal of sutures, if applicable)

Post-Op monitor will be twice a day for 5 days with notes. Antibiotic ointment may be administered per Vet Services' recommendation. TPR, attitude, activity level and appetite will be assessed; TPRs may be discontinued after the first day post-op check at vet service's discretion. In addition, the post-operative care will include 72 hr of opioid (one dose of SR buprenorphine or multiple doses of regular buprenorphine or fentanyl patch) and 72 hr of NSAID (e.g., carprofen 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr).

7. Describe how postoperative pain and distress will be assessed:

(including need for further care)

Reduced appetite and reluctant to move will indicate that Vet Services should be contacted for further assessment and potential pain alleviation.

Procedure Documents

1. Supporting documents:

Document Name Date Modified

Fig. 3: Coblation 7/22/2020 2:29 PM

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View: Custom SF: Procedure Identification

Procedure Identification: Analgesia, Buprenorphine or Buprenorphine SR (72 hours)

1. * Name of the procedure or surgery:

Analgesia, Buprenorphine or Buprenorphine SR (72 hours)

2. * Select procedure type:

Substance Administration

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research: N/A

Administration of Substances

1. * Substances:

| | Substance | Substance Scope | Route | Dose | Concentration | Volume | Substance Order for the Procedure |
|------|---|--------------------|---------------|-------------------------|---------------|--------|--|
| View | Buprenorphine HCI (Buprenex, Simbadol) | Standard | Intramuscular | 0.01 - 0.05 mg/kg | | N/A | N/A |
| View | Buprenorphine SR (Zoopharm) | Standard | Subcutaneous | 0.1 - 0.2 mg/kg | | N/A | N/A |

2. * Describe step-by-step the procedure for administering the substance(s):

For surgical procedures, buprenorphine HCl will be injected intramuscularly (IM) at least 30 minutes prior to recovery from anesthesia, and then administered every 8-12 hours for 72 hours.

For all other procedures, buprenorphine HCI will be injected intramuscularly (IM) at the time of the procedure, and then administered every 8-12 hours for 72 hours.

Alternatively, buprenorphine SR will be injected subcutaneously (SC) at the time of the procedure.

Either buprenorphine or buprenorphine SR will be given, <u>not</u> both, unless under veterinary direction.

If signs of pain are noted despite buprenorphine or buprenorphine SR administration, or following this period, Veterinary Services will be consulted.

Note: Many Category 2 or 3 procedures (e.g., laparotomies) require multimodal analgesia and more than one type of analgesic is ideally administered. Please consult with Veterinary Services if questions. Additional information can also be found in the IACUC policy on "Analgesia in Research Animals."

3. Describe the intended effects of administering the substance(s):

Provide analgesia for 72 hours.

4. Describe any potential adverse reactions to administering the substance(s):

Overdose can result in sedation and respiratory depression.

5. If working with hazardous agents, protocol personnel will read and follow the Occupational Health Recommendations (OHRs) and Biological Use Authorization letter (BUA), if applicable. The OHRs and the BUA can be found on the protocol workspace.

Needles must not be recapped unless a recapping device is used.

Gloves must be worn when handling these agents.

6. * Does this procedure include the use of a paralytic agent?

Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

View: SF: Procedure Documents

Procedure Documents

1. Supporting documents:

Document Name Date Modified

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Buprenorphine HCI (Buprenex, Simbadol)

2. Route:

Intramuscular

If you indicated Other, specify the route:

N/A

3. Dose:

0.01 - 0.05 mg/kg

4. Frequency and duration of dosages:

Once at the time of procedure, then every 8-12 hours for 72 hours

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Buprenorphine HCl is pharmaceutical grade.

8. Complication remediation:

N/A

9. Substance order for the procedure:

N/A

1. * Substance:

Buprenorphine SR (Zoopharm)

2. Route:

Subcutaneous

If you indicated Other, specify the route:

N/A

3. Dose:

0.1 - 0.2 mg/kg

4. Frequency and duration of dosages:

Once (provides approximately 72 hours of analgesia)

5. Volume (for rodents or intracranial injections):

N/A

6. Concentration:

N/A

7. Confirm the agents used will be pharmaceutical grade. If you must use non-pharmaceutical grade agents, provide scientific justification for their use and describe how the agent will be prepped and sterilized prior to use:

Buprenorphine SR is pharmaceutical grade.

8. Complication remediation:

N/A

9. Substance order for the procedure:

N/A



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Implantation

1. * Name of the procedure or surgery:

Liu-Minipig: Implantation

2. * Select procedure type:

Survival Surgery

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

i. Identify expected symptoms from administering this procedure:

Pain, swollen and possible infection around the incisions.

For pain relief and infection control, pigs will be given an opioid for a minimum of 72 hr (either a Fentanyl patch, SR buprenorphine, or regular buprenorphine) and the NSAID Carprofen for a minimum of 72 hr.

ii. Identify criteria under which animals will be removed from research:

Uncontrolled infection and > 20% loss of body weight after the procedure

Survival Surgery

1. * Surgery Type:

Major

2. * Describe how the animal, surgeon, and instruments will be prepared for surgery:

This is an aseptic surgery and will be performed in the surgical room of the animal facility. Surgeons will include the PI and his lab members. Animals will be prepared by the staff of the surgery center. All surgical instruments and implants will be autoclaved.

Animal: Animals will be fasted minimum of 12 hours before surgery. Water will be available at all times. Skin incision site(s) will be clipped of any hair, scrubbed with betadine/ chlorhexidine soap and wiped clean with alcohol for a minimum of 3 alternating wipes.

Surgeon: Surgical gown, mask and sterile surgical gloves will be worn.

3. * Describe the surgical procedure, including any deficits expected as a result of the surgery:

Aseptic surgery will be done under anesthesia and through a submandibular incision, implantation surgery will be performed. A dose of Excede (antibiotics) will be administered IM at the start of the surgery. The implants include: 1) 8 SONO crystals in the tongue base with a skin button, 2) 8 pairs of 0.1mm wire EMG electrodes with a micro-connector, and 3) 6 metal balls and 3 miniscrews.

These will be implanted into the tongue base. A small tunnel for crystal insertion will be made by a long-beaked straight hemostat via submandibular access, and the location of each crystal placement will be confirmed by trans-oral palpation. Thus, the dorsal surface of the tongue base will remain intact. These crystals are secured inside of the tongue base by their barbs. Crystals #1 and #2 will be implanted 2mm posterior to the two circumvallate papillae (boundary of the tongue base and body) and 3mm underneath the dorsal mucosa; #3 and #4 will be 25mm posterior to #1 and #2 respectively and also in the dorsal area. Crystals #5, 6, 7, 8 will be implanted in the ventral region 20mm deep to #1, 2, 3, and 4, respectively (**See Fig. 1**). These eight SONO crystals circumscribe a cubic region in which the partial glossectomy will be executed. A subcutaneous tunnel will lead the crystal and EMG wires to the location at the occipital protuberance, where the connectors will be secured by synthetic non-absorbable for non-buried skin sutures (**See Fig. 2**).

A submandibular incision along the midline will expose most of the target muscles (see below), hyoid, and thyroid cartilage. Wire bipolar electrodes (0.1mm in diameter) will be inserted via 27G hypodermic needles into the following left side muscles, and these wires will be secured by suturing to neighboring tissues: 1) Pharyngeal and hyoid muscles: superior, middle, inferior constrictors and thyrohyoideus (SC, MC, IC and TH). These muscles are responsible for the excursions of pharyngeal wall and hyoid for pushing the bolus into the esophagus, and MC and TH are indicators of both voluntary and spontaneous swallowing episodes. They are also important in other non-respiratory functions. Superior and inferior constrictors (SC and IC) will be accessed by turning the MC guide needle 45° rostrally and caudally (reaching the thyroid cartilage for the IC) respectively. 2) Palatal muscles: palatoglossus (PG), and tensor and levator veli palatini (TVP and LVP). These muscles are located at the ventral and dorsal middle and lateral sides of the soft palate. The PG elevates the tongue base and closes the oropharyngeal isthmus, and TVP and LVP tense and elevate the soft palate. Thus,

they are integral components in maintaining the patency of oropharyngeal airway and promoting swallowing. Diminished TVP activity leads to increased airway resistance. They will be directly accessed via mouth. 3) Tongue muscles: genioglossus and styloglossus (GG and SG). These two muscles are responsible for tongue protrusion and retrusion, respectively, and GG is an oropharyngeal airway dilator 4) Jaw muscles: masseter and digastricus (MA and DA). They are responsible for jaw closing and opening, respectively. The electrodes will be led out through subcutaneous tunnels. along with SONO cables (see above) and connected to a miniature connector, which will be sutured to the skin button on the back. Four 1.0 mm barbed stainless steel balls will be implanted via hypodermic syringe into the soft palate to form a square. Additional 2 balls without barbs will be embedded into small drilled holes of the hyoid bone and thyroid cartilage as reported for rabbits previously. Finally, 3 stainless steel miniscrews will be placed in the alveolar bone of right upper and lower last molars (for lateral projection) and central incisors (for axial projection). These radiopaque markers, plus the radiopaque SONO crystals, will be used to trace the shapes, positions and movements of the tongue base, soft palate, hyoid bone, thyroid cartilage, and jaw in MRI and fluoroscopic images over time.

Synthetic absorbable suture will be used for any internal (e.g., muscle, SC) layers requiring closure. Synthetic non-absorbable suture will be used for skin closure. Skin sutures will be removed by 14 days post-op, generally during a planned anesthetic event (e.g., tracking).

Possible deficits: The insertions of some EMG wire electrodes may not be hooked in the targeting muscles because of difficulty with visibility of their deep positions.

4. * Select associated substance administration procedures, including anesthesia and analgesia procedures to be used:

| Analgesia, Buprenorphine or Buprenorphine SR (72 hours) | Substance Administration | 2 Standard |
|---|-----------------------------|------------|
| Liu-Minipig: Anesthesia Protocol | Substance Administration | 1 Team |
| Liu-Minipig: Excede (ceftiofur) injection | Substance Administration | 1 Team |
| Liu-Minipig: Post-op analgesic plan | Substance Administration | 1 Team |

5. Describe how animals will be monitored during the procedure:

Animals will be monitored twice a day for 5-7 days after the procedure and post-op notes will be taken.

Vet services will monitor HR, body temperature, respiratory rate, blood pressure, and oxygen saturation.

6. Describe the routine for postoperative care: (including removal of sutures, if applicable)

lodine solution will used to clean incision areas and the area around the skin button and micro-connector daily for 7 days. Antibiotic ointment may be applied per Vet Services' recommendation. TPR, attitude, activity level

and appetite will be assessed; TPRs may be discontinued after the first day post-op check at vet service's discretion. In addition, the post-operative care will include 72 hr of opioid (one dose of SR buprenorphine or multiple doses of regular buprenorphine or fentanyl patch) and 72 hr of NSAID (e.g., carprofen 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr).

7. Describe how postoperative pain and distress will be assessed:

(including need for further care)

When the pig loses its appetite and is reluctant to move around, Vet Services will be consulted to assess the pig. Pain medication will be given per the instruction of Vet Services.

Procedure Documents

1. Supporting documents:

| Document Name | Date Modified |
|---|----------------------|
| Figs 1 and 2: SONO crystal and skin button implantation | 7/22/2020 2:28 PM |



View: Custom SF: Procedure Identification

Procedure Identification: Liu-Minipig: Soft diet

1. * Name of the procedure or surgery:

Liu-Minipig: Soft diet

2. * Select procedure type:

Special Diet

3. * Species:

Pigs - Yucatan Minipig

4. * Will administering this procedure cause any more than momentary pain or distress? Yes No

If yes,

- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

View: Custom SF: Special Diet

Special Diet

1. Composition of Diet:

Water mixed with regular pig pellet.

2. Amount:

ad lib

3. Duration:

One week after implantation surgery for all minipigs, and after tongue base volume reduction surgery for non-obese minipig in Aim 2.

4. Rodents only: verify that foods/treats (except sucrose pellets) will be autoclaved or irradiated:

Yes No

If No, provide justification here (Note: cost is not sufficient justification):

5. Intended effects on animals:

Facilitating eating.

6. Potential side-effects on animals:

None

Procedure Documents

1. Supporting documents:

Document Name Date Modified

There are no items to display

Substances Appendix:



View: Custom SF: Substance Information

Substance Information: Fentanyl (Sublimaze)

1. * Name:

Fentanyl (Sublimaze)

2. * Substance types: (select all that apply)

Analgesic

Anesthetic

Reproductive Hazard/Teratogen

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: 5-Bromodeoxyuridine (BrdU, 5-bromo-2'deoxyuridine)

1. * Name:

5-Bromodeoxyuridine (BrdU, 5-bromo-2'deoxyuridine)

2. * Substance types: (select all that apply)

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Ceftiofur sodium (Naxcel, Ceftiflex)

1. * Name:

Ceftiofur sodium (Naxcel, Ceftiflex)

2. * Substance types: (select all that apply)

Antibiotic

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Carprofen (Rimadyl)

1. * Name:

Carprofen (Rimadyl)

2. * Substance types: (select all that apply)

Analgesic

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Calcein

1. * Name:

Calcein

2. * Substance types: (select all that apply)

Other

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Buprenorphine SR (Zoopharm)

1. * Name:

Buprenorphine SR (Zoopharm)

2. * Substance types: (select all that apply)

Analgesic

Reproductive Hazard/Teratogen

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Buprenorphine HCl (Buprenex, Simbadol)

1. * Name:

Buprenorphine HCI (Buprenex, Simbadol)

2. * Substance types: (select all that apply)

Analgesic

Reproductive Hazard/Teratogen

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Saline

1. * Name:

Saline

2. * Substance types: (select all that apply)

Chemical Agent

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Vet Services Administered Anesthetics

1. * Name:

Vet Services Administered Anesthetics

2. * Substance types: (select all that apply)

Other

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions, contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display



View: Custom SF: Substance Information

Substance Information: Alizarine Complexone

1. * Name:

Alizarine Complexone

2. * Substance types: (select all that apply)

Other

3. * Is this a hazardous agent: Yes No

NOTE: Working with biohazardous agents requires a separate approval from the Institutional Biosafety Committee (IBC). Submit the Biological Use Authorization (BUA) paperwork to initiate this process. If you have questions,

contact EH&S Research and Occupational Safety at 206-221-7770 or ehsbio@uw.edu.

4. Supporting documents:

Document Name Date Modified

There are no items to display

View: Custom: Create and Edit

1. * Select the funding organization:

National Institute of Dental and Craniofacial Research (NIDCR)

If Other was selected in question 1, provide Funding Organization: $\ensuremath{\mathsf{N/A}}$

- 2. * All animal use projects must be reviewed for scientific merit prior to initiating animal use. Choose the required reviews for this project:

 Has already been conducted and approved by a funding agency
- 3. Provide name of the committee or the department reviewer (Required if "Has been conducted by my department or school and has been found to be scientifically meritorious" was selected):
 N/A
- **4. eGC1 Number(s):**(assigned internally) A146864

View: Custom: Create and Edit

Experiments Appendix:

Aim 1: To ascertain how tongue base behavior subserves respiration and swallowing

1. * Experiment name:

Aim 1: To ascertain how tongue base behavior subserves respiration and swallowing

2. * Species:

Pigs - Yucatan Minipig

3. If other was selected, provide a species:

Yucatan

4. What is the scientific goal of this experiment:

Aim 1 is to ascertain how tongue base behavior subserves respiration and swallowing and will establish a baseline for the Aim 2.

5. * Describe the animal experience in the experiment, from enrollment in the study to the final endpoint, including all procedures in chronological order and the minimum time between procedures. We encourage using bullet points, timeline, table, or a flow chart as appropriate:

Experiment one - Aim 1

Please note that the following timelines are approximate, and subject to be modified upon the detailed situation +/- 3 days.

Day 0: Pig arrival

Days 1-7: Pig's training

Day 8: Baseline recording

Day 10: Tongue impression, MRI and EUS (elastography ultrasound)

Day 12: Implantation surgery

Days 19 and 33: Longitudinal tracking

<u>Day 46:</u> Final Tongue impression, MRI and EUS (elastography ultrasound)

<u>Day 48:</u> Terminal recording. Please note that the terminal recording may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal recording.

<u>Day 48: Non-survival stimulation.</u> Will be performed immediately after the terminal recording.

Injection of cellular and bone vital labels:

- 1. BrdU will be administered *I.V.* 2 days (for activated satellite cells) and 15 days (for fusogenic ability of newly-formed myocytes) before the terminal recordings.
- 2. Flurochrome labels, Calcine and alizarin, will be injected I.V. 7 and 2 days before the terminal recording, respectively. Calcine administration will require an additional anesthetic event.

Animal Sex: Female Male

Animal Ages: 18 months

Animal Size: approximately 20-40 kg

6. Select experimental procedures:

| Name | Туре | Version | Scope |
|--|------------------------------|---------|----------|
| Anesthetic Overdose, Pentobarbital or Pentobarbital Solution | Euthanasia | 1 | Standard |
| Liu-Minipig: Food restriction | Food or Fluid Restriction | 1 | Team |
| Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE) | Imaging | 2 | Team |
| Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers | Implants | 1 | Team |
| Liu-Minipig: Stimulation | Non-Survival Surgery | 1 | Team |
| Liu-Minipig: Baseline recording | Other | 1 | Team |
| Liu-Minipig: Catheter and Wire Electrode | Other | 3 | Team |
| Liu-Minipig: Longitudinal tracking | Other | 1 | Team |
| Liu-Minipig: Pig's training | Other | 1 | Team |
| Liu-Minipig: Terminal recording | Other | 1 | Team |
| Liu-Minipig: Tongue impression | Other | 1 | Team |
| Liu-Minipig: Use of pig sling | Other | 1 | Team |
| Liu-Minipig: Barium diet | Special Diet | 2 | Team |
| Liu-Minipig: Soft diet | Special Diet | 1 | Team |

| Name | Туре | Version | Scope |
|--|-----------------------------|---------|----------|
| Analgesia, Buprenorphine or Buprenorphine SR (72 hours) | | 2 | Standard |
| Liu-Minipig: Anesthesia Protocol | Substance Administration | 1 | Team |
| Liu-Minipig: Bromodeoxyuridine (BrdU) Administration | Substance Administration | 2 | Team |
| Liu-Minipig: Excede (ceftiofur) injection | Substance Administration | 1 | Team |
| Liu-Minipig: Fluorochrome Labels for Bone | Substance Administration | 1 | Team |
| Liu-Minipig: Post-op analgesic plan | Substance Administration | 1 | Team |
| Liu-Minipig: Implantation | Survival Surgery | 1 | Team |

7. Monitoring protocol, including frequency and specific behavioral and clinical signs to be monitored. Include humane endpoints (criteria for euthanasia):

For anesthesia heart rate, corneal reflex and respiration rate, blood pressure, oxygen saturation, CO2, and temperature. Vet services will intervene when appropriate: a single apnea episode of longer than 30 seconds or O2 saturations below 80%.

Animals will be monitored for food and water intake following fasting and anesthetic events. Body weight will be monitored once a week.

Animals will be monitored at least 3 times a week by protocol personnel.

Animals are not expected to become ill, but if this occurs, we will follow the advice of Veterinary Services regarding euthanasia. In the case of the implants and surgery, we could consider euthanasia criteria to include uncontrolled infection or > 20% loss of body.

weight.

8. If there is expected mortality (spontaneous death) in this experiment:

- **a.** Procedure/condition associated with mortality: Anesthesia
- **b.** Estimated mortality rate, i.e. percentage of animals expected to die spontaneously (not via euthanasia) or need to be euthanized as a result of the procedure. (Be sure to account for this in your animal number calculations):

Less than 5%.

C. Explain why euthanasia is not possible or appropriate: N/A

9. Will some animals live out their natural lifespan as part of this experiment? If so, indicate their use and describe the monitoring plan for aged animals (e.g., rodents >18 months of age), including frequency, behavioral and clinical signs to be monitored and criteria for euthanasia.

N/A

10. * Total number of animals used in this experiment:(including all the animals to be produced)

10

a. Justify total number of animals used in this experiment:

We will use at least 18-month-old minipigs, equivalent to adult humans, because oropharyngeal disorders, such as OSA, dysphagia, and oral cancers, often occur in adults. Variability is usually larger in functional than morphological studies. Based on our previous minipig studies, the coefficients of variation of proposed benchmarks measures (see below) are approximately 20-30%. Given a conservative 1.4 to 1.6 fold ratio of means, a sample size of 7 will provide 80% power to detect a difference between these benchmark measures at a 5% significance level based on a 2-tailed Mann Whitney test. Since functional measures will be longitudinal over 5 weeks, failed recordings at certain time points are anticipated. Therefore, a sample size of 10 will be used to increase power and compensate for potential failures of recordings. No gender difference is expected, but the sample will be evenly composed of males and females to ensure that the findings apply for both sexes.

11. Number of animals by pain and distress category:(include each animal only once in the highest pain category)

B: 0

C: 0

D: 10

E: 0

a. Justify the need for any animals in pain category E:

N/A

12. * Identify husbandry exceptions:

| | Exception Type | Description and Justification |
|------|---|--|
| View | Pigs - Food treats, as outlined in the policy, are not acceptable for part or all of the study. | Food treats can be given by husbandry staff on certain days (explain below). This exemption requires an SSR. Since the food will be restricted for the reason of training. Food treats will be only given by husbandry staff during weekends and holidays when no food restriction is applied. |
| View | Pigs - Special/medicated diet | Soft diet will be provided for 5-7 day after implantation surgery. |
| View | Pigs - Special/medicated diet | Barium diet will be provided during leach recording session. |

13. Supporting documents:

Document Name

Date Modified

1. * Exception type:

Pigs - Food treats, as outlined in the policy, are not acceptable for part or all of the study.

2. Description and justification:

Food treats can be given by husbandry staff on certain days (explain below). This exemption requires an SSR.

Since the food will be restricted for the reason of training. Food treats will be only given by husbandry staff during weekends and holidays when no food restriction is applied.

1. * Exception type:

Pigs - Special/medicated diet

2. Description and justification:

Soft diet will be provided for 5-7 day after implantation surgery.

1. * Exception type:

Pigs - Special/medicated diet

2. Description and justification:

Barium diet will be provided during each recording session.

Aim 2: To evaluate how volumetric changes of the tongue base affect respiration, swallowing, and the morphology of oropharyngeal space

1. * Experiment name:

Aim 2: To evaluate how volumetric changes of the tongue base affect respiration, swallowing, and the morphology of oropharyngeal space

2. * Species:

Pigs - Yucatan Minipig

- 3. If other was selected, provide a species:
- 4. What is the scientific goal of this experiment:

Aim 2 is a longitudinal study with various interventions to determine the volume of the tongue base.

This Aim is to examine the effects of the volumetric changes of the tongue base on the respiration and swallowing. Non-obese minipigs will be used as a model of the volumetric reduction by the coblation, and Obese minipigs will be used as a model of the volumetric enlargement.

5. * Describe the animal experience in the experiment, from enrollment in the study to the final endpoint, including all procedures in chronological order and the minimum time between procedures. We encourage using bullet points, timeline, table, or a flow chart as appropriate:

Experiment two - Aim 2

Please note that the following timelines are approximate, and subject to be modified upon the detailed situation +/- 3 days.

Day 0: Pig arrival

The pig will be delivered in sibling pairs, one non-obese and one obese (BMI>50). The obese pigs will be fed a high-fat diet ad lib.

Days 1-7: Pig's training

Day 8: Baseline recording

Day 10: Tongue impression, MRI, and EUS

Day 12: Implantation surgery

Days 19: Pre-surgical baseline recording

Days 21: Pre-surgical tongue impression, MRI, and EUS

<u>Day 23:</u> Tongue base volume reduction (coblation)

Days 30 and 44: Longitudinal tracking

Day 55: Final tongue impression, MRI and EUS

<u>Day 57:</u> Terminal recording. Please note that the terminal recording may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal recording.

<u>Day 57:</u> Non-survival stimulation. Will be performed immediately after the terminal recording.

Injection of cellular and bone vital labels:

- 1. BrdU assay will be administered *I.V.* 2 days (for activated satellite cells) and 15 days (for fusogenic ability of newly-formed myocytes) before the terminal recordings.
- 2. Flurochrome labels, Calcine and alizarin, will be injected I.V. 7 and 2 days before the terminal recording, respectively. Calcine administration will require an additional anesthetic event.

| Animal | Sex |
|--------|-----|
| Female | 9 |
| Male | |

Animal Ages:

18 months

Animal Size:

25-60 kg

6. Select experimental procedures:

| Name | Туре | Version | Scope |
|--|------------------------------|---------|----------|
| Anesthetic Overdose, Pentobarbital or Pentobarbital Solution | Euthanasia | 1 | Standard |
| Liu-Minipig: Food restriction | Food or Fluid Restriction | 1 | Team |
| Liu-Minipig: MRI, elastography ultrasound (EUS), and videofluoroscopic swallowing examination (VFSE) | Imaging | 2 | Team |
| Liu-Minipig: SONO crystals, wire EMG electrodes, and metal bone markers | Implants | 1 | Team |
| Liu-Minipig: Stimulation | Non-Survival Surgery | 1 | Team |
| Liu-Minipig: Baseline recording | Other | 1 | Team |
| Liu-Minipig: Catheter and Wire Electrode | Other | 3 | Team |

| Name | Туре | Version | Scope |
|--|-----------------------------|---------|----------|
| Liu-Minipig: Longitudinal recordings | Other | 1 | Team |
| Liu-Minipig: Pig's training | Other | 1 | Team |
| Liu-Minipig: Terminal recording | Other | 1 | Team |
| Liu-Minipig: Tongue impression | Other | 1 | Team |
| Liu-Minipig: Use of pig sling | Other | 1 | Team |
| Liu-Minipig: ad lib feeding with high fat diet | Special Diet | 1 | Team |
| Liu-Minipig: Barium diet | Special Diet | 2 | Team |
| Liu-Minipig: Soft diet | Special Diet | 1 | Team |
| Analgesia, Buprenorphine or Buprenorphine SR (72 hours) | Substance Administration | 2 | Standard |
| Liu-Minipig: Anesthesia Protocol | Substance Administration | 1 | Team |
| Liu-Minipig: Bromodeoxyuridine (BrdU) Administration | Substance Administration | 2 | Team |
| Liu-Minipig: Excede (ceftiofur) injection | Substance Administration | 1 | Team |
| Liu-Minipig: Fluorochrome Labels for Bone | Substance Administration | 1 | Team |
| Liu-Minipig: Post-op analgesic plan | Substance Administration | 1 | Team |
| Liu-Minipig: Implantation | Survival Surgery | 1 | Team |
| Liu-Minipig: Tongue base reduction surgery | Survival Surgery | 1 | Team |

7. Monitoring protocol, including frequency and specific behavioral and clinical signs to be monitored. Include humane endpoints (criteria for euthanasia):

For anesthesia heart rate, corneal reflex and respiration rate, blood pressure, oxygen saturation, CO2, and temperature. Vet services will monitoring the anesthesia

Animals will be monitored for food and water intake following fasting and anesthetic events. Body weight will be monitored once a week.

Animals will be monitored at least 3 times a week by protocol personnel.

Animals are not expected to become ill, but if this were to occur, we will follow the advice of Veterinary Services regarding euthanasia. In the case of the implants and

surgery, we could consider euthanasia criteria to include uncontrolled infection or > 20% loss of body.

8. If there is expected mortality (spontaneous death) in this experiment:

a. Procedure/condition associated with mortality: Anesthesia

b. Estimated mortality rate, i.e. percentage of animals expected to die spontaneously (not via euthanasia) or need to be euthanized as a result of the procedure. (Be sure to account for this in your animal number calculations):

Less than 5%

- C. Explain why euthanasia is not possible or appropriate: Mortality would most likely occur during anesthesia for obese minipigs. Since these obese Yucatan minipigs may have spontaneous obstructive sleep apnea as verified in a previous study, there is inherent risk in allowing apnea to occur during anesthesia of non- intubated pigs (during the IV anesthesia portion of survival MRI and terminal surgery). However, this possibility is very low as none such a mortality occurred in a previous study using obese minipigs.
- 9. Will some animals live out their natural lifespan as part of this experiment? If so, indicate their use and describe the monitoring plan for aged animals (e.g., rodents >18 months of age), including frequency, behavioral and clinical signs to be monitored and criteria for euthanasia.
 N/A
- 10. * Total number of animals used in this experiment: (including all the animals to be produced)

20

a. Justify total number of animals used in this experiment:

Similar to Aim.1, the benchmarks' coefficients of variation are about 20-30% thus a 1.4 to 1.6 fold ratio of means requirs a sample size of 7 to provide 80% power for detecting a difference between partial glossectomy and obesity groups at a 5% significance level using a 2-tailed Mann-Whitney test. As stated in Aim 1, sample size of each group (both sexes) will be 10 to compensate potential failures of chronic recordings over 5 weeks. An effort will be made to test animals in sibling sets of the same sex: one receives the coblation for volume reduction, and another receives a special feeding regime for obesity.

11. Number of animals by pain and distress category:(include each animal only once in the highest pain category)

B: 0

C: 0

D: 20

E: 0

a. Justify the need for any animals in pain category E:

N/A

12. * Identify husbandry exceptions:

| | Exception Type | Description and Justification |
|------|---|--|
| View | Pigs - Food treats, as outlined in the policy, are not acceptable for part or all of the study. | Food treats can be given by husbandry staff on certain days (explain below). This exemption requires an SSR. Since the food will be restricted for the reason of training. Food treats will be only given by husbandry staff during weekends and holidays when no food restriction is applied. |
| View | Pigs - Special/medicated diet | Barium diet will be provided during each recording session. Ad lib feeding will be applied for obese minipigs with a high fat diet. |
| View | Pigs - Special/medicated water | Soft diet will be provided for 5-7 day after implantation and tongue base volume reduction surgeries. |

13. Supporting documents:

Document Name Date Modified

There are no items to display

1. * Exception type:

Pigs - Food treats, as outlined in the policy, are not acceptable for part or all of the study.

2. Description and justification:

Food treats can be given by husbandry staff on certain days (explain below). This exemption requires an SSR.

Since the food will be restricted for the reason of training. Food treats will be only given by husbandry staff during weekends and holidays when no food restriction is applied.

1. * Exception type:

Pigs - Special/medicated diet

2. Description and justification:

Barium diet will be provided during each recording session.

Ad lib feeding will be applied for obese minipigs with a high fat diet.

1. * Exception type:

Pigs - Special/medicated water

2. Description and justification:

Soft diet will be provided for 5-7 day after implantation and tongue base volume reduction surgeries.

View: Custom: Add Vivarium Location

1. * Identify the location where animals will be used:

Brotman ABSL1

a. For locations that are lab managed, provide justification for housing outside of the vivarium:

N/A

2. * What species will be housed in this location?

| Common Name | Scientific Name |
|------------------------|-----------------|
| | |
| Pigs - Yucatan Minipig | Sus scrofa |

View: UW IACUC Select Room Level

1. Campus:

Vivarium

2. Vivarium:

Brotman Vivarium

3. * BSL Level:

Brotman ABSL1

View: Custom: Add Vivarium Location

1. * Identify the location where animals will be used:

ARCF ABSL1

a. For locations that are lab managed, provide justification for housing outside of the vivarium:

Housing relocation for all USDA large animals

2. * What species will be housed in this location?

| Common Name | Scientific Name | |
|------------------------|-----------------|--|
| | | |
| Pigs - Yucatan Minipig | Sus scrofa | |

View: UW IACUC Select Room Level

1. Campus:

Vivarium

2. Vivarium:

ARCF (Animal Research & Care Facility)

3. * BSL Level:

ARCF ABSL1

View: Custom: Add Animal Use Location

1. * Identify the location where animals will be used:

ARCF ABSL1

a. For locations that are outside of the vivarium, provide justification for the use of this space:

N/A

2. * What species will be used in this location?

| Common Name | Scientific Name |
|------------------------|-----------------|
| Pigs - Yucatan Minipig | Sus scrofa |

3. Describe how this location will be used:

All surgical procedures and recording sessions

4. * If animals are left unattended in this location, provide an explanation and include maximum duration:

Animals will not be left unattended.

5. Describe how animals will be transported to and from this location, including container and route. (Note: use of private vehicles requires IACUC approval):

On a cart within the vivarium, DCM van for between SLU and HSB.

View: UW IACUC Select Room Level

1. Campus:

Vivarium

2. Vivarium:

ARCF (Animal Research & Care Facility)

3. * BSL Level:

ARCF ABSL1

View: Custom: Add Animal Use Location

1. * Identify the location where animals will be used:

Brotman ABSL1

a. For locations that are outside of the vivarium, provide justification for the use of this space:

N/A

2. * What species will be used in this location?

| Cor | nmon Name | Scientific Name | |
|-----|---------------------|-----------------|--|
| Pig | s - Yucatan Minipig | Sus scrofa | 1400004 0000000000000000000000000000000 |

3. Describe how this location will be used:

MRI

4. * If animals are left unattended in this location, provide an explanation and include maximum duration:

Animals will not be left unattended.

5. Describe how animals will be transported to and from this location, including container and route. (Note: use of private vehicles requires IACUC approval):

On a cart within the vivarium, DCM van for between SLU and HSB.

View: UW IACUC Select Room Level

1. Campus:

Vivarium

2. Vivarium:

Brotman Vivarium

3. * BSL Level:

Brotman ABSL1

From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 10, 2020 10:57 PM

To: Zi-Jun Liu

Subject: Protocol revisions

Hi Zee,

I went over your responses and found that there were several questions from the vet that were not addressed. I tried to respond on your behalf for some of them, but one that you will have to do is:

- 1) In the two surgery procedures, you will need to create and add Substance Administration procedures for the Fentanyl patch (for dose say that vet services will determine correct patch size/dose) and the Carprofen, which is an NSAID (for carprofen dose, put: 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr).
- 2) Then you will have to add both of these new Substance Administration procedures to Q4 of the two surgery procedures.

Also, I wanted to let you know that on the Procedure Personnel Assignment page, I removed Michael Baldwin from the list of personnel to perform the Surgeries because he doesn't have the required certification to do surgery solo on USDA species.

Once you have completed #1 and #2 above, I will double-check it and send your responses back to the vet.

Thanks, Michelle From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Thursday, August 6, 2020 9:34 AM

To: Nicholas L. Reyes; Michelle Brot; Gary A. Fye

Subject: Re: Animal Protocol

Nick,

Thank you so much for your prompt reply. Would you please let me know when the Vet review would be completed?

Zee

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Thursday, August 6, 2020 9:01 AM

To: Zi-Jun Liu <zjliu@uw.edu>; Michelle Brot <mbrot@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: Animal Protocol

Morning Zee,

I believe your protocol is still in the vet review process. We discussed anesthesia and that info has been relayed to the OAW but Vet Services does not perform your protocol review. That process is still ongoing.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Thursday, August 6, 2020 8:58 AM

To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: Animal Protocol

Michelle,

I checked again, the protocol still remains in the Box "Pre-review". Do the Vet Serivces need to take some action to move it forward?

Zee

From: Michelle Brot <mbrot@uw.edu> **Sent:** Wednesday, August 5, 2020 1:28 PM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Re: Animal Protocol

Yes, Zee, we're aware of your time crunch and are moving it along as fast as we can.

Regards, Michelle

From: Zi-Jun Liu <zjliu@uw.edu>

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Thank you for your quick reply. The UW SOP sent me an email today again to request the Just-in-Time materials. As soon as this animal protocol is approved, I will be able to the package of JIT package to the UW SOP.

Niranjan will complete the training soon.

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Wednesday, August 5, 2020 12:59 PM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Re: Animal Protocol

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Take care, Michelle

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France Michaella Breat (mchaet@uu. adu.)

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To: Michelle Brot <mbrot@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>, "Gary A. Fye"

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Sent: Thursday, August 6, 2020 10:44 AM **To:** Michelle Brot; Nicholas L. Reyes

Subject: Re: Animal Protocol

Thank you, Michelle.

The notice from both NIDCR and UW SOP was sent more than a month aga, and the SOP sent another one yesterday. So far, I have not been told the deadline for the submission of JIT.

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Regards,

Michelle

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Thursday, August 6, 2020 9:33 AM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Michelle Brot <mbrot@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: Animal Protocol

Nick,

Thank you so much for your prompt reply. Would you please let me know when the Vet review would be completed?

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To: Zi-Jun Liu <zjliu@uw.edu>; Michelle Brot <mbrot@uw.edu>; Gary A. Fye <gfye@uw.edu>

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Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Thursday, August 6, 2020 8:58 AM

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To: Michelle Brot <mbrot@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 10:43:58 AM Subject: Re: Animal Protocol

Thank you, Michelle.

The notice from both NIDCR and UW SOP was sent more than a month aga, and the SOP sent another one yesterday. So far, I have not been told the deadline for the submission of JIT.

Zee

From: Michelle Brot <mbrot@uw.edu> **Sent:** Thursday, August 6, 2020 9:54 AM

To: Zi-Jun Liu <zjliu@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

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Sent: Thursday, August 20, 2020 12:00 PM

To: Nicholas L. Reyes

Subject: Re: another Zee Liu protocol Q

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Sound reasonable?

Or if you have an idea for something more specific, I'm open to that, too.

Thanks, Molly

From: Molly K. Lucas

Sent: Wednesday, August 19, 2020 12:21 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Subject: another Zee Liu protocol Q

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Link to

protocol: https://hoverboard.washington.edu/Hoverboard/sd/Rooms/DisplayPages/LayoutInitial? Container=com.webridge.entity.Entity[OID[BBD9E52211666B4AB9BA57EE24AED8CC]] From: Molly K. Lucas <mklucas@uw.edu>
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I think if we suggest a plan (with specific language), he will probably accept it... at least that's how it's been working for my other suggestions. I've been doing more direct editing than I normally do. These surgeries are just a little more difficult for me to envision compared to a laparatomy or something.

Please let me know what you think, e.g., good language to include for the closures (I usually expect it to say how many layers and general type of suture, e.g., "synthetic non-absorbable," but does not need to list suture size).

Thanks, Molly

Link to

protocol: https://hoverboard.washington.edu/Hoverboard/sd/Rooms/DisplayPages/LayoutInitial? Container=com.webridge.entity.Entity[OID[BBD9E52211666B4AB9BA57EE24AED8CC]]

From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/20/2020 12:00:16 PM

Subject: Re: another Zee Liu protocol Q

I've been mulling this over and one option is to keep it relatively vague, e.g.,

"Synthetic absorbable suture will be used for any internal (e.g., muscle, SC) layers requiring closure. Synthetic non-absorbable suture will be used for skin closure. Skin sutures will be removed by 14 days post-op, generally during a planned anesthetic event (e.g., tracking)."

Sound reasonable?

Or if you have an idea for something more specific, I'm open to that, too.

Thanks, Molly

From: Molly K. Lucas

Sent: Wednesday, August 19, 2020 12:21 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu> **Subject:** another Zee Liu protocol Q

Hi Nick,

It turns out I saw another thing that was missing - both survival surgeries were lacking detail re: closures.

In response to my comment asking for more detail (and giving our recommendation of synthetic nonabs for non-buried sutures and synthetic absorbable for buried), he added this to the implant surgery: "Finally, the submandibular incision will be closed with synthetic non-absorbable for non-buried skin sutures."

And this to the tongue reduction surgery (which will have a skin incision overlying the masseter muscle in addition to the tongue): "Finally, the incision will be closed with synthetic non-absorbable for non-buried skin sutures without layers." for the skin, and this for the tongue, "The lesion will be closed with absorbable sutures in 2-3 layers (See Fig. 3: Coblation)."

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To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/7/2020 10:49:37 AM

Subject: Re: follow up analgesia question

Attach: [Liu Z 8 5 20.docx]

Thanks Nick. Here's a copy of the comments I just entered into Hoverboard, updated after our conversation yesterday.

Now I have that rabbit sinusitis new protocol waiting in my inbox. It wasn't ready for vet consult yet when we did it in protocol review class. I need to refamiliarize myself with it, but there's a good chance I may want to discuss that one with you as well... maybe next week?

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Friday, August 7, 2020 10:20 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: follow up analgesia question

Hey Molly,

If we could leave the patch size up the discretion of VS that would be great....and the carprofen dosing sounds correct.

Thanks! Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Thursday, August 6, 2020 4:49 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu> **Subject:** follow up analgesia question

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Please comment/edit as needed.

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Please edit as needed to ensure that the plan is described consistently throughout the protocol/procedures.

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From: Molly K. Lucas <mklucas@uw.edu>
Sent: Friday, August 7, 2020 10:50 AM

To: Nicholas L. Reyes

Subject: Re: follow up analgesia question

Attachments: Liu_Z_8_5_20.docx

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From: Leandra Mosca lmosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/7/2020 10:15:34 AM Subject: Re: Liu Pig Anesthesia

Hey Nick, 1pm on Monday works. Thank you so much and I really apologize. Someone still needed to sign off on Megan teaching Sx 1A.

Leandra

On Aug 7, 2020, at 9:11 AM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

I have a few meetings this afternoon starting at 1pm so might not give us enough time. Wanna push until Monday? I could make 1pm on Monday work. Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Leandra Mosca < Imosca@uw.edu> **Sent:** Friday, August 7, 2020 8:36 AM **To:** Nicholas L. Reyes < nlreyes@uw.edu>

Subject: RE: Liu Pig Anesthesia

Hi Nick,

Would it be possible to bump our meeting back to 12:40p? I had to switch into an AUTS class today that goes until 12:30p.

Thanks, Leandra

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 11:39 AM **To:** Leandra Mosca <lmosca@uw.edu>

Subject: Re: Liu Pig Anesthesia

How about noon. That work?

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

nlreyes@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Thursday, August 6, 2020 11:26 AM To: Nicholas L. Reyes < lmosca@uw.edu >

Subject: RE: Liu Pig Anesthesia

Hi Nick,

Thanks! I am available any time tomorrow. Mid-morning to afternoon would be ideal (if possible) since I'm doing some cell work in the morning- but I can definitely work with your schedule

Thank you, Leandra

From: Nicholas L. Reyes <<u>nlreyes@uw.edu</u>>
Sent: Thursday, August 6, 2020 8:12 AM
To: Leandra Mosca <<u>lmosca@uw.edu</u>>

Subject: Re: Liu Pig Anesthesia

Hey Leandra,

Great job. Let's definitely get together to discuss. I have a couple suggestions based on previous experience with similar experiments. When would be a good day/time to zoom. FYI I did send Zee the attachment doc which outlines our many porcine drug options. Not sure if you've seen this doc already but its somewhat of an overkill formulary that IACUC approves for pig procedures wherein VS will run all anesthesia. By approving the blanket formulary it lets us adjust on the fly (I attached it here for your reference). The doc that you are working on will be for our internal use so we have a little time to finalize it. Let me know when you can meet.

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Dept. of Comparative Medicine

University of Washington, Seattle

nlreyes@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Wednesday, August 5, 2020 3:14 PM To: Nicholas L. Reyes < nirryes@uw.edu>

Subject: Liu Pig Anesthesia

Hi Nick,

I have attached my summary/recommendations for the Liu pig project.

The pigs do not need sedation or restraint for removing equipment after recording—I confirmed with Zee.

Should we discuss this when you are available?

Thanks, Leandra

Leandra Mosca, DVM
Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772

From: Leandra Mosca <mosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

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Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

nlreves@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Wednesday, August 5, 2020 3:14 PM To: Nicholas L. Reyes < lmosca@uw.edu >

Subject: Liu Pig Anesthesia

Hi Nick,

I have attached my summary/recommendations for the Liu pig project.

The pigs do not need sedation or restraint for removing equipment after recording—I confirmed with Zee.

Should we discuss this when you are available?

Thanks, Leandra

Leandra Mosca, DVM
Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772

From: Leandra Mosca lmosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 11:44:44 AM Subject: RE: Liu Pig Anesthesia

Sounds great! I'll email a Zoom link tomorrow.

Thanks, Leandra

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 11:39 AM **To:** Leandra Mosca <lmosca@uw.edu>

Subject: Re: Liu Pig Anesthesia

How about noon. That work?

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

nlreyes@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu
Sent: Thursday, August 6, 2020 11:26 AM
To: Nicholas L. Reyes < lmosca@uw.edu

Subject: RE: Liu Pig Anesthesia

Hi Nick,

Thanks! I am available any time tomorrow. Mid-morning to afternoon would be ideal (if possible) since I'm doing some cell work in the morning- but I can definitely work with your schedule

Thank you, Leandra From: Nicholas L. Reyes <nlreyes@uw.edu>
Sent: Thursday, August 6, 2020 8:12 AM
To: Leandra Mosca <lmosca@uw.edu>
Subject: Re: Liu Pig Anesthesia

Hey Leandra,

Great job. Let's definitely get together to discuss. I have a couple suggestions based on previous experience with similar experiments. When would be a good day/time to zoom. FYI I did send Zee the attachment doc which outlines our many porcine drug options. Not sure if you've seen this doc already but its somewhat of an overkill formulary that IACUC approves for pig procedures wherein VS will run all anesthesia. By approving the blanket formulary it lets us adjust on the fly (I attached it here for your reference). The doc that you are working on will be for our internal use so we have a little time to finalize it. Let me know when you can meet.

Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

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Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772

From: Leandra Mosca <mosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 11:26:42 AM Subject: RE: Liu Pig Anesthesia

Hi Nick,

Thanks! I am available any time tomorrow. Mid-morning to afternoon would be ideal (if possible) since I'm doing some cell work in the morning- but I can definitely work with your schedule

Thank you, Leandra

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 8:12 AM **To:** Leandra Mosca <lmosca@uw.edu>

Subject: Re: Liu Pig Anesthesia

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Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

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Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772

From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 24, 2020 4:13 PM
To: Andrew Burich; Molly K. Lucas
Subject: Re: Liu Pig Swallowing Protocol

Hi Andrew,

Thanks for your thorough review of this and your eagle eyes! I think Molly and I both had reviewer fatigue by the time we were done so clearly we missed editing the surgery procedures. The explanation is that Molly suggested that since Vet Services retains discretion on how they want to proceed with the pig anesthesia, it would be best (and consistent with other large animal procedures) to have an attached list of every possible anesthetic agent that might be used and have the procedure refer to that. That change was made for at experiment level but hadn't been caught within the surgery procedures. I will go ahead and make the swap so that the <u>Substance Administration: Liu-Minipig: Anesthesia Protocol (Team)</u> procedure replaces the Vet Services Administered Anesthetics procedure.

Feel free to get in touch if you find any more inconsistencies (I promise, we didn't hide them for you intentionally!! ©

~Michelle

From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Monday, August 24, 2020 3:19 PM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Liu Pig Swallowing Protocol

Hey there,

Before I ask the PI this question, I thought maybe you could help me out.

This is for Aim 1, but may apply to Aim 2: I noticed that in **Survival Surgery: Liu-Minipig: Implantation (Team)** he lists on pg2, Q4 a procedure for Vet Services Administered Anesthetics. However, this is completely different than **Substance Administration: Liu-Minipig: Anesthesia Protocol (Team)** that is in the Procedure List.

Which is correct? The one in the survival surgery procedure needs to be edited because it talks about sleep devices.

I'd like to "thank" the person that assigned me this protocol. ©

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA
Director, Animal Resources
Benaroya Research Institute at Virginia Mason
1201 Ninth Avenue | Seattle, WA 98101
p 206.342.6967
BenaroyaResearch.org

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From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Monday, August 31, 2020 10:27 AM

To: Michelle Brot

Subject: RE: Liu Pig Swallowing Protocol

HI Michelle,

I need to pass this back to you to work with Zee on getting this protocol in shape. I am spending way too much time with this and I have other amendments in my inbox to review.

Briefly,

he added a special diet procedure for high fat chow for the pigs based on one of my questions....then he removed it. However, if you look in Aim 2 Husbandry Exceptions – when talking about barium he mentions a high fat diet. So not sure if the pigs are or aren't being fed a high fat diet.

Also, for some reason, he changed his "Other: Liu-Minipig: Terminal recording (Team)" into "Behavioral Testing (with Food or Fluid Restriction): Liu-Minipig: Terminal recording, ver. 1 (Team)".

I'd be grateful if you could help with this.

Thanks,

Α

Andrew J. Burich, DVM, MS, DACLAM, CPIA

Director, Animal Resources
Benaroya Research Institute at Virginia Mason
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BenaroyaResearch.org

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, August 24, 2020 4:13 PM

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From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 31, 2020 10:44 AM

To: Andrew Burich

Subject: Re: Liu Pig Swallowing Protocol

Sure thing, Andrew. I really appreciate your thorough review since you caught some issues that Molly and I hadn't seen. I also spent way too much time on this protocol and am happy to see it through and be done with it. I will work with him to get your final questions resolved.

Take care, Michelle

From: Andrew Burich <aburich@benaroyaresearch.org>

Sent: Monday, August 31, 2020 10:26 AM **To:** Michelle Brot <mbrot@uw.edu> **Subject:** RE: Liu Pig Swallowing Protocol

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From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Tuesday, July 7, 2020 9:07 AM
To: Michelle Brot; stephh26
Subject: Re: New animal protocol

Stephanie and Michelle,

I am so grateful for your very timely and efficient helps on this. Hopefully, the review process would be quick, and I would be able to submit the Just-in-Time materials and get the fund in time.

Thank you so much again,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Tuesday, July 7, 2020 8:41 AM

To: stephh26 <stephh26@uw.edu>; Zi-Jun Liu <zjliu@uw.edu>

Subject: Re: New animal protocol

Thanks for you help with this, Stephanie! Let the reviewing begin!!

① Michelle

From: stephh26 < stephh26@uw.edu> Sent: Tuesday, July 7, 2020 8:32 AM

To: Michelle Brot <mbrot@uw.edu>; Zi-Jun Liu <zjliu@uw.edu>

Subject: RE: New animal protocol

Hi Zee and Michelle.

I'll go ahead and submit this new protocol to start the review process and Zee won't have to wait until Wednesday.

Best, Stephanie

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, July 6, 2020 6:44 PM

To: Zi-Jun Liu <zjliu@uw.edu>; stephh26 <stephh26@uw.edu>

Subject: Re: New animal protocol

Hi Zee

I removed the offending procedure and it looks like it's able to be submitted now. Feel free to do so at your convenience.

Best wishes, Michelle

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Monday, July 6, 2020 4:19 PM

To: stephh26 <<u>stephh26@uw.edu</u>>; Michelle Brot <<u>mbrot@uw.edu</u>>

Subject: Re: New animal protocol

Stephanie and Michelle,

Thank you for your great helps. There will be no live sleep monitoring in the project. So, this procedure should be removed.

Since I must get prepared for tomorrow's NIDCR study section meeting for reviewing grants, I will get back to the animal protocol on Wed if there is anything needing to do before the submission.

Thank you again,

Zee

From: stephh26 < stephh26@uw.edu > Sent: Monday, July 6, 2020 8:19 AM

Subject: RE: New animal protocol

Hi Zee and Michelle.

It looks like Liu- Minipig: The placement of the AASM level II portable sleep monitoring device (Embletta MPR PG, Embla Systems, Ontario, Canada) was archived to create Liu- Minipig: The placement of the Bioradio system.

Are these the same procedure? If this is not the same procedure, I would recommend you to copy the archived version then add this new copy back into the protocol. If this is the same procedure, you will need to switch out the old one with the new one.

You can let me know which you prefer and I can switch out procedures and submit the protocol. Unfortunately I cannot submit if there are errors as well. Please let me know if you have

any additional questions.

Also, I wanted to let you know Dr. Weaver has been added to HoverBoard and should be selectable now.

Sincerely, Stephanie

Stephanie Huang

Program Operations Specialist
Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oawrss@uw.edu / oaw.washington.edu

W UNIVERSITY of WASHINGTON



Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Michelle Brot <<u>mbrot@uw.edu</u>>
Sent: Monday, July 6, 2020 5:29 AM
To: Zi-Jun Liu <<u>zjliu@uw.edu</u>>
Cc: stephh26 <<u>stephh26@uw.edu</u>>
Subject: Re: New animal protocol

Hi Zee

Yes Stephanie will probably get back to us this morning.

Sent from my iPhone

On Jul 6, 2020, at 1:25 AM, Zi-Jun Liu <zjliu@uw.edu> wrote:

Hello Michelle,

Thank you for your quick check. this new project has 3 specific aims but Aim 3 is histology. So, I did Aims 1 and 2 in this new animal protocol. I really don't know how to fix these problems. Would Stephanie be able to help with the submission?

Zee

From: Michelle Brot <mbrot@uw.edu>

Sent: Saturday, July 4, 2020 6:32 PM

To: Zi-Jun Liu <zjliu@uw.edu>; stephh26 <stephh26@uw.edu>

Subject: Re: New animal protocol

Hi Zee,

I found 2 archived procedures; one you had a newer version so I just replaced it with that. The other is "Other: Liu- Minipig: The placement of the AASM level II portable sleep monitoring device (Embletta MPR PG, Embla Systems, Ontario, Canada) (Team)[Archived]."

 $I\ can't\ find\ a\ newer\ version\ of\ that\ one\ so\ I\ would\ like\ Stephanie\ to\ look\ into\ why\ it's\ considered\ Archived.$

In any case, Zee, I don't think you have to correct these before submitting the protocol. See if you can try again. If it doesn't allow you to Submit, I think Stephanie can do it for you.

Take care, Michelle

From: Zi-Jun Liu <<u>zjliu@uw.edu</u>> Sent: Friday, July 3, 2020 2:16 PM

To: stephh26 <<u>stephh26@uw.edu</u>>; Michelle Brot <<u>mbrot@uw.edu</u>>

Subject: Re: New animal protocol

Hello Stephanie and Michelle,

I have pretty much done the new protocol. However, when I clicked the submit button, the following error message pumped up, I just don't know to delete outdated procedures. Would you please advise?

2 procedures associated with this protocol have newer versions.

Outdated procedures must be replaced before the next triennial review can be submitted

Thank you very much,

Zee

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Friday, July 3, 2020 9:51 AM To: stephh26 <stephh26@uw.edu> Cc: Michelle Brot < mbrot@uw.edu > Subject: Re: New animal protocol

Stephanie

Thank you for the explanation. Dr. Weaver's UW ID is "eweaver" I will add him later on after he complete the training.

I will renew the medical screen.

Zee

From: stephh26 <stephh26@uw.edu>
Sent: Thursday, July 2, 2020 2:25 PM
To: Zi-Jun Liu <ziliu@uw.edu>
Cc: Michelle Brot <mbrot@uw.edu>
Subject: RE: New animal protocol

Hi Zee,

It looks like Dr. Weaver does not have an account in HoverBoard yet. Accounts are created after completion of required animal training. I have created an account for him. Can you let me know his UW NetID?

Please note, Dr. Weaver will need to complete animal training before he can be approved on a protocol. You can visit our Animal Use Training site or contact auts@uw.edu directly if you have any training questions.

Additionally, it looks like your Animal Use Medical Screening is has expired. You can visit the previous link to submit a form and renew it.

Kind regards, Stephanie

Stephanie Huang

Program Operations Specialist
Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oaw.washington.edu

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From: Zi-Jun Liu <<u>zjliu@uw.edu</u>> Sent: Thursday, July 2, 2020 2:17 PM To: stephh26 <<u>stephh26@uw.edu</u>> Cc: Michelle Brot <<u>mbrot@uw.edu</u>> Subject: Re: New animal protocol

Stephanie,

This is great. Just one quick question, one of my Co-Is, Dr. Edward Weaver of Head and neck surgery in SoM will help with tongue surgery but I was unable to add him because I could not locate his organization. Would you please let me know what to do in this case?

Zee

From: stephh26 <stephh26@uw.edu> Sent: Thursday, July 2, 2020 2:10 PM To: Zi-Jun Liu <ziliu@uw.edu> Cc: Michelle Brot <mbrot@uw.edu> Subject: RE: New animal protocol

Hi Zee,

This one is copied from the old one and is already a new protocol in pre-submission. After you are done editing, you can click the "Submit" button and it will send it to our office for review. The old protocol is still in HoverBoard.

If you have questions while filling out the protocol, feel free to reach out to Michelle. As a reviewer, she will know much more than me about how to answer those questions.

Best, Stephanie

Stephanie Huang Program Operations Specialist

Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oawrss@uw.edu / oaw.washington.edu

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Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Zi-Jun Liu <<u>zijliu@uw.edu</u>>
Sent: Thursday, July 2, 2020 2:04 PM
To: stephh26 <<u>stephh26@uw.edu</u>>
Co: Michelle Brot <<u>mbrot@uw.edu</u>>
Subject: Re: New animal protocol

Stephanie,

Thank you. Now, I can edit this expired protocol but not sure if this revised protocol would turn to be a new protocol. Would you please advise?

Zee

From: stephh26 <stephh26@uw.edu>
Sent: Thursday, July 2, 2020 1:04 PM
To: Zi-Jun Liu <2||iu@uw.edu>
Cc: Michelle Brot <mbrot@uw.edu>
Subject: RE: New animal protocol

Hi Zee,

Congratulations on receiving funding!

I cannot revive the protocol, but copying and editing it is an option. It will receive a new protocol number. I have copied the submission for you here: Obstructive Sleep Apnea — An Obese Minipig Model. Please let me know if you are unable to access.

You may find it easier to create a new protocol instead. If that is the case, you can discard this submission and create a new protocol from scratch.

Feel free to let me or Michelle know if you have any additional HoverBoard questions.

Kind regards, Stephanie

Stephanie Huang

Program Operations Specialist Office of Animal Welfare Research Support Services

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From: Michelle Brot <<u>mbrot@uw.edu</u>> Sent: Thursday, July 2, 2020 11:03 AM

To: Zi-Jun Liu <zjliu@uw.edu>; stephh26 <stephh26@uw.edu>

Subject: Re: New animal protocol

Hi Zee,

That's wonderful news about your grant being funded...Congratulations! Regarding you -04 protocol, it looks like you closed it a couple years ago (literally to the day!!) but I am cc'ing Stephanie Huang in our office to see if she can re-open it or make it available to you by copying it. I have my fingers crossed on that. If she can do that and you want to work on editing it but need help, it might be best for us to work on it over the phone. We can set up a time to talk if you need my help.

Best wishes, Michelle

From: Zi-Jun Liu <<u>zjliu@uw.edu</u>>
Sent: Thursday, July 2, 2020 10:54 AM
To: Michelle Brot <<u>mbrot@uw.edu</u>>

Subject: Re: New animal protocol

Hello Michelle,

I was able to access my previous protocol (3393-04) in HoverBoard, but I don't know how to revise this protocol and make it as a new one. Would you please give me some instruction? I actually called the Animal Welfare Office but the gentleman I talked to does not know what to do as well.

Sorry for bother you again,

Zee

From: Zi-Jun Liu

Sent: Thursday, July 2, 2020 10:32 AM

To: Michelle Brot < mbrot@uw.edu Subject: New animal protocol

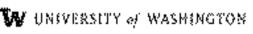
Hello Michelle,

Thank you so much for your great helps on my animal protocols.

About two weeks ago, I was informed that NIDCR will fund my new R01 grant reviewed late last year. Now, I received the notice that the Just-in-Time materials must be submitted as soon as possible. Therefore, I have to get the new animal protocol done and have it to be approved as quickly as possible. Since the study still uses minipigs and most of procedures would be more or less similar to the previous protocol on OSA obese minipig model, I would like to access the previous protocol (3393-04) and make relevant changes on that. Unfortunately, I totally forgot how to use the Hoverboard. Would I get your helps again?

Thank you so much,

Zee





From: Michelle Brot <mbrot@uw.edu>
Sent: Tuesday, July 7, 2020 9:08 AM
To: Zi-Jun Liu; stephh26
Subject: Re: New animal protocol

I'll try to review it soon, Zee, and get you any questions I have.

Take care, Michelle

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Tuesday, July 7, 2020 9:07 AM

To: Michelle Brot <mbrot@uw.edu>; stephh26 <stephh26@uw.edu>

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From: stephh26 < stephh26@uw.edu>
Sent: Tuesday, July 7, 2020 8:32 AM
To: Michalle Brot < mbrot@uw.edu>: 7i-Jun Liu < ziliu

To: Michelle Brot <mbrot@uw.edu>; Zi-Jun Liu <zjliu@uw.edu>

Subject: RE: New animal protocol

Hi Zee and Michelle,

I'll go ahead and submit this new protocol to start the review process and Zee won't have to wait until Wednesday.

Best, Stephanie

From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, July 6, 2020 6:44 PM
To: 7i-Jun Liu < zijiu@uw edu>: stenbh26 < ste

To: Zi-Jun Liu <zjliu@uw.edu>; stephh26 <stephh26@uw.edu>

Subject: Re: New animal protocol

Hi Zee,

I removed the offending procedure and it looks like it's able to be submitted now. Feel free to do so at your convenience.

Best wishes, Michelle

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Monday, July 6, 2020 4:19 PM

Subject: Re: New animal protocol

Stephanie and Michelle,

Thank you for your great helps. There will be no live sleep monitoring in the project. So, this procedure should be removed.

Since I must get prepared for tomorrow's NIDCR study section meeting for reviewing grants, I will get back to the animal protocol on Wed if there is anything needing to do before the submission.

Thank you again,

Zee

From: stephh26 < stephh26@uw.edu > Sent: Monday, July 6, 2020 8:19 AM

To: Michelle Brot <mbrot@uw.edu>; Zi-Jun Liu <zjliu@uw.edu>

Subject: RE: New animal protocol

Hi Zee and Michelle,

It looks like Liu- Minipig: The placement of the AASM level II portable sleep monitoring device (Embletta MPR PG, Embla Systems, Ontario, Canada) was archived to create Liu- Minipig: The placement of the Bioradio system.

Are these the same procedure? If this is not the same procedure, I would recommend you to copy the archived version then add this new copy back into the protocol. If this is the same procedure, you will need to switch out the old one with the new one.

You can let me know which you prefer and I can switch out procedures and submit the protocol. Unfortunately I cannot submit if there are errors as well. Please let me know if you have any additional questions.

Also, I wanted to let you know Dr. Weaver has been added to HoverBoard and should be selectable now.

Sincerely, Stephanie

Stephanie Huang

Program Operations Specialist Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oawrss@uw.edu / oaw.washington.edu

W UNIVERSITY of WASHINGTON D2C

Compassion Fatigue

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, July 6, 2020 5:29 AM To: Zi-Jun Liu <zjliu@uw.edu> Cc: stephh26 <stephh26@uw.edu> Subject: Re: New animal protocol

Hi Zee

Yes Stephanie will probably get back to us this morning.

Sent from my iPhone

On Jul 6, 2020, at 1:25 AM, Zi-Jun Liu <ziliu@uw.edu> wrote:

Hello Michelle,

Thank you for your quick check. this new project has 3 specific aims but Aim 3 is histology. So, I did Aims 1 and 2 in this new animal protocol. I really don't know how to fix these problems. Would Stephanie be able to help with the submission?

Zee

From: Michelle Brot <mbrot@uw.edu>

Sent: Saturday, July 4, 2020 6:32 PM

To: Zi-Jun Liu <zjliu@uw.edu>; stephh26 <stephh26@uw.edu>

Subject: Re: New animal protocol

I found 2 archived procedures; one you had a newer version so I just replaced it with that. The other is "Other: Liu- Minipig: The placement of the AASM level II portable sleep monitoring device (Embletta MPR PG, Embla Systems, Ontario, Canada) (Team)[Archived]."

I can't find a newer version of that one so I would like Stephanie to look into why it's considered Archived.

In any case, Zee, I don't think you have to correct these before submitting the protocol. See if you can try again. If it doesn't allow you to Submit, I think Stephanie can do it for you.

Take care, Michelle

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Friday, July 3, 2020 2:16 PM

To: stephh26 <stephh26@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: New animal protocol

Hello Stephanie and Michelle,

I have pretty much done the new protocol. However, when I clicked the submit button, the following error message pumped up, I just don't know to delete outdated procedures. Would you please advise?

2 procedures associated with this protocol have newer versions.

Outdated procedures must be replaced before the next triennial review can be submitted

Thank you very much,

Zee

From: Zi-Jun Liu <ziliu@uw.edu>
Sent: Friday, July 3, 2020 9:51 AM
To: stephh26 <stephh26@uw.edu>
Cc: Michelle Brot <mbrot@uw.edu>
Subject: Re: New animal protocol

Stephanie

Thank you for the explanation. Dr. Weaver's UW ID is "eweaver" I will add him later on after he complete the training.

I will renew the medical screen.

Zee

From: stephh26 < stephh26@uw.edu>
Sent: Thursday, July 2, 2020 2:25 PM
To: Zi-Jun Liu < ziliu@uw.edu>
Ce: Michelle Brot < mbrot@uw.edu>
Subject: RE: New animal protocol

Hi Zee

It looks like Dr. Weaver does not have an account in HoverBoard yet. Accounts are created after completion of required animal training. I have created an account for him. Can you let me know his UW NetID?

Please note, Dr. Weaver will need to complete animal training before he can be approved on a protocol. You can visit our Animal Use Training site or contact auts@uw.edu directly if you have any training questions.

Additionally, it looks like your Animal Use Medical Screening is has expired. You can visit the previous link to submit a form and renew it.

Kind regards, Stephanie

Stephanie Huang

Program Operations Specialist
Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oawrss@uw.edu / oaw.washington.edu

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Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Zi-Jun Liu <zijliu@uw.edu> Sent: Thursday, July 2, 2020 2:17 PM To: stephh26 <stephh26@uw.edu> Cc: Michelle Brot <mbrot@uw.edu> Subiect: Re: New animal protocol

Stephanie,

This is great. Just one quick question, one of my Co-Is, Dr. Edward Weaver of Head and neck surgery in SoM will help with tongue surgery but I was unable to add him because I could not locate his organization. Would you please let me know what to do in this case?

Zee

From: stephh26 <stephh26@uw.edu>
Sent: Thursday, July 2, 2020 2:10 PM
To: Zi-Jun Liu <ziliu@uw.edu>
Cc: Michelle Brot <mbrot@uw.edu>
Subject: RE: New animal protocol

Hi Zee.

This one is copied from the old one and is already a new protocol in pre-submission. After you are done editing, you can click the "Submit" button and it will send it to our office for review. The old protocol is still in HoverBoard.

If you have questions while filling out the protocol, feel free to reach out to Michelle. As a reviewer, she will know much more than me about how to answer those questions.

Best, Stephanie

Stephanie Huang

Program Operations Specialist

Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oawrss@uw.edu / oaw.washington.edu

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Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Zi-Jun Liu <<u>zjilu@uw.edu</u>>
Sent: Thursday, July 2, 2020 2:04 PM
To: stephh26 <<u>stephh26@uw.edu</u>>
Co: Michelle Brot <<u>mbrot@uw.edu</u>>
Subject: Re: New animal protocol

Stephanie,

Thank you. Now, I can edit this expired protocol but not sure if this revised protocol would turn to be a new protocol. Would you please advise?

Zee

From: stephh26 < stephh26@uw.edu>
Sent: Thursday, July 2, 2020 1:04 PM
To: Zi-Jun Liu < ziliu@uw.edu>
Ce: Michelle Brot < mbrot@uw.edu>
Subject: RE: New animal protocol

Hi Zee,

Congratulations on receiving funding!

I cannot revive the protocol, but copying and editing it is an option. It will receive a new protocol number. I have copied the submission for you here: Obstructive Sleep Apnea — An Obese Minipig Model. Please let me know if you are unable to access.

You may find it easier to create a new protocol instead. If that is the case, you can discard this submission and create a new protocol from scratch.

Feel free to let me or Michelle know if you have any additional HoverBoard questions.

Kind regards, Stephanie

Stephanie Huang

Program Operations Specialist
Office of Animal Welfare Research Support Services

Health Sciences Building Box 357160 1705 NE Pacific Street Seattle, WA 98195-7160 206.685.3988 fax 206.616.1297 oaw.washington.edu

<Outlook-cid_B9B480.png> <Outlook-cid_081AB8.png>

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Michelle Brot < mbrot@uw.edu > Sent: Thursday, July 2, 2020 11:03 AM

To: Zi-Jun Liu <<u>zjliu@uw.edu</u>>; stephh26 <<u>stephh26@uw.edu</u>>

Subject: Re: New animal protocol

Hi Zee,

That's wonderful news about your grant being funded...Congratulations! Regarding you -04 protocol, it looks like you closed it a couple years ago (literally to the day!!) but I am cc'ing Stephanie Huang in our office to see if she can re-open it or make it available to you by copying it. I have my fingers crossed on that. If she can do that and you want to work on editing it but need help, it might be best for us to work on it over the phone. We can set up a time to talk if you need my help.

Best wishes, Michelle

From: Zi-Jun Liu <<u>zjiliu@uw.edu</u>>
Sent: Thursday, July 2, 2020 10:54 AM
To: Michelle Brot <<u>mbrot@uw.edu</u>>
Subject: Re: New animal protocol

Hello Michelle,

I was able to access my previous protocol (3393-04) in HoverBoard, but I don't know how to revise this protocol and make it as a new one. Would you please

give me some instruction? I actually called the Animal Welfare Office but the gentleman I talked to does not know what to do as well.

Sorry for bother you again,

Zee

From: Zi-Jun Liu

Sent: Thursday, July 2, 2020 10:32 AM
To: Michelle Brot <mbrot@uw.edu>
Subject: New animal protocol

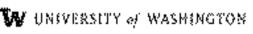
Hello Michelle,

Thank you so much for your great helps on my animal protocols.

About two weeks ago, I was informed that NIDCR will fund my new R01 grant reviewed late last year. Now, I received the notice that the Just-in-Time materials must be submitted as soon as possible. Therefore, I have to get the new animal protocol done and have it to be approved as quickly as possible. Since the study still uses minipigs and most of procedures would be more or less similar to the previous protocol on OSA obese minipig model, I would like to access the previous protocol (3393-04) and make relevant changes on that. Unfortunately, I totally forgot how to use the Hoverboard. Would I get your helps again?

Thank you so much,

Zee





From: Nicholas L. Reyes <nlreyes@uw.edu>
Sent: Tuesday, August 4, 2020 11:52 AM

To: VET SERVICES PROTOCOL REVIEW; Zi-Jun Liu

Cc: Michelle Brot; achris08; Leandra Mosca; Gary A. Fye; Molly K. Lucas

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Attachments: Attachment A-MANUAL OF STANDARD OPERATING PROCEDURES.NR edit

12.14.18.docx

Hello Zee.

I touched base with Michelle Brot regarding the best way to add in our anesthetic plan for your protocol. Because VS will be running and maintain anesthesia for all of your experiments you can go ahead and add our pig anesthesia attachment document. This includes way more anesthetic options than we are likely to use but gives us the flexibility to adjust based on our experiences. I've attached the current version of this doc to this email. Leandra is still working on our specific plan for your experiments, but we will keep that version internal for our preparation for you experiments in the fall or winter. Below are instructions from Michelle on how to add this anesthetic procedure into hoverboard. Please let her know if you have any questions regarding wording.

Add a procedure called "<u>Vet Services Administered Anesthestics</u>" which refers to an attachment at the end of the procedure that lists all potential anesthetics that may be used in a surgery or other procedure for that species. Here is what it says in Herring's Q2 "Describe step-by-step the procedure for administering the substance(s):" for the anesthetics administration procedure "Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended."

Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

France VET CERVICES PROTOCOL REVIEW Associate Constant

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Wednesday, July 29, 2020 8:39 AM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Please see the zoom invitation below for tomorrow at 10AM. Looking forward to meeting you.

221.122.88.195 (China)

213.19.144.110 (EMEA)

115.114.131.7 (India Mumbai) 115.114.115.7 (India Hyderabad)

DCM is inviting you to a scheduled Zoom meeting.

```
Join Zoom Meeting
                                                              RCW 42.56.420(4)
https://washington.zoom.us/j/
Meeting ID:
One tap mobile
                              # US (Seattle)
+12063379723,
+12532158782,
                              # US (Tacoma)
Dial by your location
    +1 206 337 9723 US (Seattle)
    +1 253 215 8782 US (Tacoma)
    +1 971 247 1195 US (Portland)
    +1 213 338 8477 US (Los Angeles)
    +1 346 248 7799 US (Houston)
    +1 602 753 0140 US (Phoenix)
    +1 669 219 2599 US (San Jose)
    +1 669 900 6833 US (San Jose)
    +1 720 928 9299 US (Denver)
    +1 470 250 9358 US (Atlanta)
    +1 470 381 2552 US (Atlanta)
    +1 646 518 9805 US (New York)
    +1 646 876 9923 US (New York)
    +1 651 372 8299 US (St. Paul)
    +1 786 635 1003 US (Miami)
    +1 267 831 0333 US (Philadelphia)
    +1 301 715 8592 US (Germantown)
    +1 312 626 6799 US (Chicago)
Meeting ID:
Find your local number: <a href="https://washington.zoom.us/u/aADpJbh5Q">https://washington.zoom.us/u/aADpJbh5Q</a>
Join by SIP
              @zoomcrc.com
Join by H.323
162.255.37.11 (US West)
162.255.36.11 (US East)
```

103.122.166.55 (Australia) 209.9.211.110 (Hong Kong SAR) 64.211.144.160 (Brazil) 69.174.57.160 (Canada) 207.226.132.110 (Japan)

Meeting ID:

RCW 42.56.420(4)

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Tuesday, July 28, 2020 9:21 PM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <Imosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu> **Subject:** Re: New R01 grant - Anesthesia for Liu Pigs

Alex,

Yes, please send me the meeting invitation.

Thanks,

Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 28, 2020 4:42 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thanks for getting back to us. Can you meet this Thursday at 10AM via zoom?

Thanks,

Alex

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, July 27, 2020 9:34 PM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Alex,

Thanks for your mail. I am pretty flexible this week for a Zoom meeting to discuss the anesthetic procedures for my new project. Please let me know when the meeting will be set up.

Looking forward to getting your helps with anesthetic procedures.

Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Monday, July 27, 2020 4:43 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <Imosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hi Zee,

Just wanted to follow up with you about discussing your anesthesia plan for your new protocol.

Can you reply with your availability so we can arrange zoom meeting to discuss?

Thank you, Alexandra Christodoulou, DVM Veterinary resident

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 21, 2020 3:00 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <Imosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thank you for reaching out to vet services for protocol review. Dr. Nick Reyes, Dr. Leandra Mosca, and myself would like to set up a Zoom meeting to discuss your anesthetic plan for the minipigs in your new protocol.

Do you have time later this week on either Thursday or Friday to talk with us?

And please don't hesitate to let me know if you have any additional questions.

Best,

Alex

Alexandra Christodoulou, DVM Veterinary Resident From: Zi-Jun Liu <zjliu@uw.edu> Sent: Tuesday, July 21, 2020 10:29 AM To: Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu> Cc: Michelle Brot <mbrot@uw.edu> Subject: Re: New RO1 grant - Anesthesia for Liu Pigs Gary, Great, Thank you so much, Zee From: Gary Fye <gfye@u.washington.edu> Sent: Tuesday, July 21, 2020 10:17 AM To: Zi-Jun Liu <zjliu@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu> Subject: Re: New R01 grant - Anesthesia for Liu Pigs Morning Zi, I have added our protocol review to this email. A veterinarian will contact you to discuss the anesthesia for your project. Thanks, Gary On Tue, Jul 21, 2020 at 10:12 AM Zi-Jun Liu <zjliu@uw.edu> wrote: Hello, Gary, Thank you for providing info about MRI and x-ray C-Arm machine. I am working on the animal protocol with IACUC. I have been using the anesthetic procedures created by the Vet Service for my previous project on OSA obese minipigs. Would you please let me know who I should ask for reviewing these anesthetic procedures or if you would be able to review them? Best regards, Zee

--

Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington

Attachment A

MANUAL OF STANDARD OPERATING PROCEDURES

Anesthesia/Analgesia of the Pig

University of Washington

Center for Videoendoscopic Surgery

Seattle, WA, 98195-6410

I. Introduction/Purpose

A. The purpose of this SOP is to provide appropriate dose ranges for a variety of anesthetic and analgesic drug options which may be utilized by Vet Services staff for the induction and maintenance of anesthesia in pigs.

II. Procedures

- A. General: The CVES animal lab is administered by the Department of Surgery to provide accredited animal surgical care for training and research animals. The Director of CVES is the faculty member in charge.
- B. The following anesthetic drug regimen is the most common protocol used by CVES:
 - 1. Preanesthesia: Glycopyrrolate .01 mg/kg
 - 2. Induction: Telazol 1-5.5 mg/kg I.M.; Xylazine 1-5.5 mg/kg I.M.
 - 3. Maintenance: Isoflurane 1% 3%
- C. Other drug dosages used for anesthesia/analgesia in pig:

1. Preanesthetics:

- a. Glycopyrrolate .01 mg/kg
- b. Atropine .02-.05 mg/kg I.M. Atropine is injected 10-15 minutes before endotracheal intubation to dry bronchial secretions and prevent bradycardia due to vagal stimulation.
- c. Diazepam 2 mg/kg I.M. Best when used in combination with Ketamine.
- d. Diazepam 2 mg/kg I.M.: Ketamine 10 mg/kg I.M.
- e. Acepromazine 0.2 mg/kg I.M. May produce hypotension and bradycardia. Do not give more than 15 mg/pig.
- f. Droperidol 2 mg/kg I.V., 4 mg/kg I.M.
- g. Ketamine 20-33 mg/kg I.M.
- h. Butorphanol 0.1-0.3mg/kg: Xylazine 1-4mg/kg I.M.
- i. Midazolam 0.1-0.5mg/kg (can be used alone as premedication sedation or in combination with butorphanol and/or xylazine as doses listed in h.)

2. Dissociative agents and combinations:

a. Ketamine 11-33 mg/kg I.M., I.V. Increases intracranial pressure. Poor muscle relaxation.

Increases heart rate and blood pressure and decreases

- cardiac contractility. Use with caution in animals with hepatic and renal disease.
- b. Ketamine 22-33 mg/kg: Acetylpromazine 1.1 mg/kg I.M.
- c. Ketamine 15 mg/kg: Diazepam 2 mg/kg I.M.
- d. Ketamine 20 mg/kg: Xylazine 2 mg/kg I.M.
- e. Ketamine 11 mg/kg: Fentanyl-Droperidol 1mL/14kg I.M.
- f. Ketamine 15 mg/kg: Azaperone 2 mg/kg I.M.
- g. Ketamine 2 mg/kg: Xylazine 2 mg/kg: Oxymorphone .075 mg/kg I.V. (2x dose for I.M.)
- h. Ketamine 20 mg/kg: Climazolam .5-1.0 mg/kg I.M.
- i. Tiletamine-Zolazepam (Telazol) 4-6 mg/kg I.M.
- j. Tiletamine-Zolazepam (Telazol) 4-6 mg/kg: Xylazine 2.2 mg/kg I.M.
- k. "G-K-X": 5% guaifenesin-0.1% ketamine-0.1%xylazine in 5% dextrose solution: 1mg ketamine, 1mg xylazine and 50mg guaifenesen per mL of 5% dextrose solution.
 - i. G-K-X induction bolus: 1 ml/kg I.V.
 - ii. G-K-X maintenance infusion: 1-4ml/kg/hr I.V.

3. Barbiturates:

- a. Pentobarbital 20-40 mg/kg I.V.; 5-15 mg/kg/hr continuous I.V. infusion. May cause some respiratory depression and sedation, and may induce histamine release resulting in peripheral vasodialation. May delay gastric emptying, increase intestinal peristalsis and cause spasm of biliary tract.
- b. Thiopental 6.6-25 mg/kg I.V., 50-100 mcg/kg/min (3-6 mg/kg/hr) continuous I.V. infusion rate. May cause some respiratory depression and sedation, and may induce histamine release resulting in peripheral vasodialation. May delay gastric emptying, increase intestinal peristalsis and cause spasm of biliary tract.
- c. Thiamylal 6.6-25 mg/kg I.V., 50-100 mcg/kg/min (3-6 mg/kg/hr) continuous I.V. infusion rate. May cause some respiratory depression and sedation, and may induce histamine release resulting in peripheral vasodialation. May delay gastric emptying, increase intestinal peristalsis and cause spasm of biliary tract.

4. Inhalants:

- a. Methoxyflurane: Slowest to change anesthetic level in patient; 45% metabolized.
- b. Isoflurane: Fastest to change anesthetic level in patient; 0.2% metabolized.

5. Miscellaneous injectable restraint agents:

- a. Azaperone 2.2 mg/kg I.M.
- b. Chloralose 55-86 mg/kg I.V.
- c. Etomine 4-8 mg/kg I.V.
- d. Etorphine/Acetylpromazine (Imobilon) .245 mg/10 kg: Diprenorphine (Revivon) .3 mg/kg
- e. Midazolam 100-500 mcg/kg I.M.; Can be combined with propofol (5.g.) and/or fentanyl (6.b.) at a dose of 0.4-0.7 mg/kg/hr as a continuous I.V. infusion for maintenance of anesthesia.
- f. Metomidate 4 mg/kg I.V.
- g. Propofol 0.83-1.66 mg/kg I.V. bolus; 12-20 mg/kg/hr continuous I.V. infusion.
- h. Alflaxalone:
 - i. Induction at 0.47-1mg/kg IV or 1-10 mg/kg IM
 - ii. Maintenance CRI at 0.1-0.3 mg/kg/min +/-xylazine at 0.04ug/kg/min

6. Analgesics:

- a. Fentanyl .02-.05 mg/kg I.M. q2h.
- b. Fentanyl 30-100 mcg/kg/hour I.V. drip.
- c. Sufentanyl 5-10 mcg/kg I.M. q2h.
- d. Sufentanyl 10-30 mcg/kg/hour I.V. drip.
- e. Buprenorphine .005-.02 mg/kg I.M. or I.V. q6-12h.
- f. Butorphanol .1-.3 mg/kg I.M. q 4-6h.
- g. Meperidine 2-10 mg/kg I.M. q4h
- h. Oxymorphone .15 mg/kg I.M. q4h
- i. Pentazocine 1.5-3.0 mg/kg I.M. q4h
- j. Phenylbutazone 10-20 mg/kg P.O. q12h.
- k. Aspirin 10 mg/kg P.O. q4h.

7. Miscellaneous drugs:

- a. Respiratory arrest: (1) Doxapram 1-4 mg/kg I.V. May produce respiratory alkalosis and hyperkalemia. Overdose causes convulsions.
- b. Cardiac arrest:
 - (1) Epinephrine 6-10 .g/kg I.C. or 20-30 .g/kg I.V. (.1-.2 mL/20 kg). Increases heart rate and cardiac output. Causes intense vasoconstriction of renal and splanchnic vasculature. Arrhythmogenic
 - (2) Isoproterenol 1-6 .g/kg I.C. or 2-10 g/kg I.V. Increases heart rate

and cardiac output. Lowers mean arterial blood pressure, requiring concurrent blood volume expansion. Arrhythmogenic.

- c. Antiarrhythmics:
 - (1) Atropine 10-40 g/kg I.V. May cause excessive tachycardia. May predispose to sympathetic-induced arrhythmias.
 - (2) Glycopyrrolate .005-.01 mg/kg I.V. May cause excessive tachycardia.
 - (3) Lidocaine 2-4 mg/kg I.V. 50 mcg/kg/min. continuous I.V. infusion.
 - (4) Bretylium tosylate 3.0-5.0 mg/kg I.V. q30 min.
- d. Bradycardia: (1) Atropine .05 mg/kg I.V.
- e. Calcium channel blockers: (1) Diltiazem 2-4 mg/kg P.O. TID.
 - f. Coronary vasorelaxant: (1) Nitroglycerine 200 mcg diluted in 2 ml saline and infused slowly into coronary sinus.
 - g. Anticholinergic: (1) Atropine .05 mg/kg I.M.; .02 mg/kg I.V.
 - h. Malignant hyperthermia treatment and prophylaxis: (1) Dantrolene 5 mg/kg/ I.V.

III. References

Swindle, MM. Anesthetic and Perioperative Techniques in Swine: An Update. Technical Bulletin. Charles River Laboratories, Spring 1994.

Muir, WWIII, Hubbell, JAE. 1989. Handbook of Veterinary Anesthesia. The C. V. Mosby Company, St. Louis, Missouri.

Clecknell, PA, 1987. Laboratory Animal Anesthesia Academic Press, Inc., San Diefo, California.

Tumbleson, Me, 1986. Swine in Biomedical Research, Vol. 1. Plenum Press, New York, New York.

Suckow, MA, 1988. The University of Michigan Swine Notes.

Last edited by N. Reyes 12.14.18

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Tuesday, August 4, 2020 12:52 PM **To:** Nicholas L. Reyes; Michelle Brot

Cc: achris08; Leandra Mosca; Gary A. Fye; Molly K. Lucas; VET SERVICES PROTOCOL

REVIEW

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Nick and Michelle,

Nick, thank you so much for your quick helps on the anesthetic procedure. Does this indicate that the Vet Services Protocol Review has been completed?

Michelle, would you please unlock the protocol, so I can add "<u>Vet Services Administered Anesthestics</u>" as a new procedure?

Thank you again,

Zee

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Tuesday, August 4, 2020 11:52 AM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>; Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Gary A.

Fye <gfye@uw.edu>; Molly K. Lucas <mklucas@uw.edu> Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

I touched base with Michelle Brot regarding the best way to add in our anesthetic plan for your protocol. Because VS will be running and maintain anesthesia for all of your experiments you can go ahead and add our pig anesthesia attachment document. This includes way more anesthetic options than we are likely to use but gives us the flexibility to adjust based on our experiences. I've attached the current version of this doc to this email. Leandra is still working on our specific plan for your experiments, but we will keep that version internal for our preparation for you experiments in the fall or winter. Below are instructions from Michelle on how to add this anesthetic procedure into hoverboard. Please let her know if you have any questions regarding wording.

Add a procedure called "<u>Vet Services Administered Anesthestics</u>" which refers to an attachment at the end of the procedure that lists all potential anesthetics that may be used in a surgery or other procedure for that species. Here is what it says in Herring's Q2 "**Describe step-by-step the procedure for administering the substance(s):**" for the anesthetics administration procedure "Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended."

Thanks,

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Wednesday, July 29, 2020 8:39 AM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee.

Please see the zoom invitation below for tomorrow at 10AM. Looking forward to meeting you.

Best,

Alex

DCM is inviting you to a scheduled Zoom meeting.

Join Zoom Meeting

https://washington.zoom.us/j/

Meeting ID:

One tap mobile

+12063379723,, # US (Seattle)

+12532158782,, # US (Tacoma)

Dial by your location

+1 206 337 9723 US (Seattle)

+1 253 215 8782 US (Tacoma)

+1 971 247 1195 US (Portland)

+1 213 338 8477 US (Los Angeles)

+1 346 248 7799 US (Houston)

+1 602 753 0140 US (Phoenix)

+1 669 219 2599 US (San Jose)

+1 669 900 6833 US (San Jose)

+1 720 928 9299 US (Denver)

+1 470 250 9358 US (Atlanta)

+1 470 381 2552 US (Atlanta)

RCW 42.56.420(4)

+1 646 518 9805 US (New York) +1 646 876 9923 US (New York) +1 651 372 8299 US (St. Paul) +1 786 635 1003 US (Miami) RCW 42.56.420(4) +1 267 831 0333 US (Philadelphia) +1 301 715 8592 US (Germantown) +1 312 626 6799 US (Chicago) Meeting ID: Find your local number: https://washington.zoom.us/u/aADpJbh5Q Join by SIP @zoomcrc.com Join by H.323 162.255.37.11 (US West) 162.255.36.11 (US East) 221.122.88.195 (China) 115.114.131.7 (India Mumbai) 115.114.115.7 (India Hyderabad) 213.19.144.110 (EMEA) 103.122.166.55 (Australia) 209.9.211.110 (Hong Kong SAR) 64.211.144.160 (Brazil) 69.174.57.160 (Canada) 207.226.132.110 (Japan) Meeting ID: From: Zi-Jun Liu <zjliu@uw.edu> Sent: Tuesday, July 28, 2020 9:21 PM To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu> Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <Imosca@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu> Subject: Re: New R01 grant - Anesthesia for Liu Pigs Alex, Yes, please send me the meeting invitation. Thanks, Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 28, 2020 4:42 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thanks for getting back to us. Can you meet this Thursday at 10AM via zoom?

Thanks,

Alex

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, July 27, 2020 9:34 PM

To: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Alex,

Thanks for your mail. I am pretty flexible this week for a Zoom meeting to discuss the anesthetic procedures for my new project. Please let me know when the meeting will be set up.

Looking forward to getting your helps with anesthetic procedures.

Zee

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Monday, July 27, 2020 4:43 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <Imosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hi Zee,

Just wanted to follow up with you about discussing your anesthesia plan for your new protocol.

Can you reply with your availability so we can arrange zoom meeting to discuss?

Thank you,
Alexandra Christodoulou, DVM
Veterinary resident

From: VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Sent: Tuesday, July 21, 2020 3:00 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>; achris08 <achris08@uw.edu>; Leandra Mosca <lmosca@uw.edu>; Nicholas

L. Reyes <nlreyes@uw.edu>; Gary A. Fye <gfye@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Hello Zee,

Thank you for reaching out to vet services for protocol review. Dr. Nick Reyes, Dr. Leandra Mosca, and myself would like to set up a Zoom meeting to discuss your anesthetic plan for the minipigs in your new protocol.

Do you have time later this week on either Thursday or Friday to talk with us?

And please don't hesitate to let me know if you have any additional questions.

Best,

Alex

Alexandra Christodoulou, DVM Veterinary Resident

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Tuesday, July 21, 2020 10:29 AM

To: Gary A. Fye <gfye@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Cc: Michelle Brot <mbrot@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Gary,

Great, Thank you so much,

Zee

From: Gary Fye <gfye@u.washington.edu> Sent: Tuesday, July 21, 2020 10:17 AM

To: Zi-Jun Liu <zjliu@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu>

Subject: Re: New R01 grant - Anesthesia for Liu Pigs

Morning Zi,

I have added our protocol review to this email. A veterinarian will contact you to discuss the anesthesia for your project.

Thanks, Gary

| (| On Tue, Jul 21, 2020 at 10:12 AM Zi-Jun Liu < <u>zjliu@uw.edu</u> > wrote: |
|---|---|
| | Hello, Gary, |
| | Thank you for providing info about MRI and x-ray C-Arm machine. |
| | I am working on the animal protocol with IACUC. I have been using the anesthetic procedures created by the Vet Service for my previous project on OSA obese minipigs. Would you please let me know who I should ask for reviewing these anesthetic procedures or if you would be able to review them? |
| | Best regards, |

Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington

To: "Gary A. Fye" <gfye@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 7/3/2020 9:45:15 PM

Subject: Re: new R01 grant for Liu - MRI

Thanks for sending Gary. Have a happy 4th

Get Outlook for iOS

From: Gary Fye <gfye@u.washington.edu> Sent: Friday, July 3, 2020 1:19:07 PM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Brian M. Iritani <biritani@uw.edu>

Subject: Fwd: new R01 grant for Liu - MRI

FYI...looking to get rolling at ARC by the end of the year.

Gary

----- Forwarded message ------From: **Zi-Jun Liu** <<u>zjliu@uw.edu</u>>
Date: Fri, Jul 3, 2020 at 12:27 PM
Subject: Re: new R01 grant - MRI
To: Gary A. Fye <gfye@uw.edu>

Gary,

This is an anther good resource. I will contact the contact person to see the availability of the use for minipigs.

This project will use the total of 30 18-month-old Yucatan minipigs with either genders, 10 for Aim 1 (normal ones) and 20 for Aim 2 (10 normal for tongue base volume reduction and 10 obese for tongue base volume enlargement.

Zee

From: Gary Fye <gfye@u.washington.edu> Sent: Friday, July 3, 2020 10:44 AM

To: Zi-Jun Liu <zjliu@uw.edu>
Cc: Gary A. Fye <gfye@uw.edu>
Subject: Re: new R01 grant - MRI

Morning Zi,

There is an MRI for research in Health Sciences. See this link.

https://rad.washington.edu/research/equipment/

Also curious, how many pigs on your new project? You plan to use SPF or farm pigs?

Gary



Virus-free. www.avast.com

On Fri, Jul 3, 2020 at 9:30 AM Zi-Jun Liu <<u>ziliu@uw.edu</u>> wrote:

Gary,

Just have one more question. Do you know if MRI scan on minipigs could be done in the main campus here? As you knew, we did these scans in the south campus, but the animal transportation has always been complicated and headache.

Thank you again,

Zee

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Friday, July 3, 2020 9:15 AM

To: Gary A. Fye <gfye@uw.edu>; Levin, Dmitry <dlevin@cardiology.washington.edu>

Subject: Re: new R01 grant - Fluoroscope Available?

Hello Gary,

Thank you so much for your quick reply and long-standing support on my research.

I would be much easier for me to carry out this experiment if it can be done in the ARC.

Dmitry, would you please confirm this as I am now preparing animal protocol and needing this info.

Thank you very much,

Zee

From: Gary Fye <gfye@u.washington.edu>

Sent: Thursday, July 2, 2020 3:30 PM

To: Zi-Jun Liu <zjliu@uw.edu>; Levin, Dmitry <dlevin@cardiology.washington.edu>

Cc: Gary A. Fye <gfye@uw.edu>

Subject: Re: mew R01 grant - Fluoroscope Available?

Afternoon Zi,

Congrats on your new grant!

I have added Dmitry Levin who does have a fluoroscope here in Health Sciences. I believe it is

available for rent with him running the machine but he can elaborate. DCM can run the anesthesia for the pig at ARC and the machine is portable so can be moved there.

Let me know if you need any other assistance and have a good weekend.

Gary

On Thu, Jul 2, 2020 at 2:19 PM Zi-Jun Liu <<u>zjliu@uw.edu</u>> wrote: Hello Gary,

My new R01 will be funded by the NIDCR soon and I am now preparing the animal protocol. One major procedure for this new project is to take x-ray fluoroscopy on live minipigs during swallowing with barium and respiration. I remembered that you mentioned that the Vet Services may have the machine in the facility. Would you please let me know if I can do this in the animal facility by then (late this year) , or this procedure will have to be performed in the South Lake campus as I did previously?

Thank you very much,

Zee

Gary Fye, LVT
Program Operations Specialist
Veterinary Services

Veterinary Services
University of Washington

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Gary Fye, LVT
Program Operations Specialist
Veterinary Services
University of Washington



Virus-free. www.avast.com

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Gary Fye, LVT Program Operations Specialist Veterinary Services University of Washington From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 17, 2020 10:16 AM

To: Zi-Jun Liu

Subject: Re: Protocol 3393-05

Thanks, Zee. I'll send it back to them for re-review.

~Michelle

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Monday, August 17, 2020 10:14 AM

To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: Protocol 3393-05

Michelle,

I have addressed all comments/questions by the secondary review from the Vet Services. I hope this would make the process move forward.

Thank you,

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Wednesday, August 19, 2020 9:25 AM

To: Michelle Brot

Subject: Re: Protocol 3393-05

Hello Michelle,

Want is the current status of the protocol review?

Thank you,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, August 17, 2020 10:15 AM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Re: Protocol 3393-05

Thanks, Zee. I'll send it back to them for re-review.

~Michelle

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Monday, August 17, 2020 10:14 AM

To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; VET SERVICES PROTOCOL REVIEW

<vsreview@uw.edu>

Subject: Re: Protocol 3393-05

Michelle,

I have addressed all comments/questions by the secondary review from the Vet Services. I hope this would make the process move forward.

Thank you,

From: Zi-Jun Liu <zjliu@uw.edu>

To: Michelle Brot <mbrot@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>, VET SERVICES

PROTOCOL REVIEW <vsreview@uw.edu>

Sent: 8/17/2020 10:14:37 AM **Subject:** Re: Protocol 3393-05

Michelle,

I have addressed all comments/questions by the secondary review from the Vet Services. I hope this would make the process move forward.

Thank you,

From: Michelle Brot <mbrot@uw.edu> Sent: Wednesday, August 19, 2020 9:32 AM To: Zi-Jun Liu **Subject:** Re: Protocol 3393-05 Hi Zee The vets are reviewing your response to their last set of questions. If they re satisfied it will go to the IACUC. Take care Michelle On Aug 19, 2020, at 9:26 AM, Zi-Jun Liu <zjliu@uw.edu> wrote: Hello Michelle, Want is the current status of the protocol review? Thank you, Zee From: Michelle Brot <mbrot@uw.edu> Sent: Monday, August 17, 2020 10:15 AM To: Zi-Jun Liu <zjliu@uw.edu> Subject: Re: Protocol 3393-05 Thanks, Zee. I'll send it back to them for re-review. ~Michelle From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, August 17, 2020 10:14 AM To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>; VET SERVICES PROTOCOL REVIEW <vsreview@uw.edu> Subject: Re: Protocol 3393-05 Michelle,

I have addressed all comments/questions by the secondary review from the Vet Services. I hope this would make the process move forward.

Thank you,

From: Michelle Brot <mbrot@uw.edu>

Sent: Wednesday, August 12, 2020 12:30 PM

To: Zi-Jun Liu

Subject: Re: Protocol revisions

Hi Zee,

Once the vets are satisfied with your responses, it will take a week for the IACUC to review the protocol. The vets are reviewing your answers now (could take a day or two) so we'll know more once we hear back from them. I'd estimate 1.5 weeks or so.

Take care, Michelle

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Wednesday, August 12, 2020 12:23 PM

To: Michelle Brot <mbrot@uw.edu> **Subject:** Re: Protocol revisions

Hello Michelle,

The NIDCR award has come to the UW OSP. So, they are requesting the proof of the compliance of animal use again. Would you please let me know how long the approval process would be taking roughly?

Thank you,

Zee

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Tuesday, August 11, 2020 9:17 AM **To:** Michelle Brot <mbrot@uw.edu> **Subject:** Re: Protocol revisions

Michelle,

I did some revisions in the two surgeries per your instruction.

I tried to remove Niranjan Balu, Daniel Leotta, and Jeffrey Thiel from all substance administration and post-op analgesic plan, but it does not look successful. Would you please help on this?

Thank you very much for your prompt replies and helps always,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, August 10, 2020 10:57 PM **To:** Zi-Jun Liu <zjliu@uw.edu> **Subject:** Protocol revisions

Hi Zee,

I went over your responses and found that there were several questions from the vet that were not addressed. I tried to respond on your behalf for some of them, but one that you will have to do is:

- 1) In the two surgery procedures, you will need to create and add Substance Administration procedures for the Fentanyl patch (for dose say that vet services will determine correct patch size/dose) and the Carprofen, which is an NSAID (for carprofen dose, put: 2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr).
- 2) Then you will have to add both of these new Substance Administration procedures to Q4 of the two surgery procedures.

Also, I wanted to let you know that on the Procedure Personnel Assignment page, I removed Michael Baldwin from the list of personnel to perform the Surgeries because he doesn't have the required certification to do surgery solo on USDA species.

Once you have completed #1 and #2 above, I will double-check it and send your responses back to the vet.

From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Tuesday, September 1, 2020 10:32 AM

To: Michelle Brot

Subject: RE: Still need some questions answered.....

Hello Michelle,

I really appreciate all of your helps and advices over the long-course of this animal protocol reviewing. I am sure your helps are still needed during the course of this new research project.

Best regards,

Zee

From: Michelle Brot [mailto:mbrot@uw.edu] Sent: Monday, August 31, 2020 2:18 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Subject: Still need some questions answered.....

Hi Zee,

The IACUC reviewer wanted me to check with you on a couple items:

1) Are the obese pigs in Aim 2 going to be fed a high fat diet while they are at UW? If so, the Special Diet procedure that you created needs to be added back into the list of procedures and this needs to be mentioned in Q5 of Exp 002. If not, the second sentence in the Q12 Husbandry exceptions for the Special/medicated Diet needs to be removed:

Pigs - Barium diet will be provided during each recording session. Ad lib feeding Special/medicated diet will be applied for obese minipigs with a high fat diet.

- 2) In Aim 01, Q5, it says "Day 48: Terminal recording. *Please note that the terminal surgery may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal surgery.*" and there is the same sentence in Aim 2 for Day 57.
- a) Is the "terminal surgery" the same as the "Stimulation Surgery"? You need to refer to it in Q5 as you call it in the Procedure Name.
- b) When I read about the Terminal Recording procedure in "Behavioral Testing: Terminal Recording (w/Food Restriction)", it says that Terminal Recording is the same as Longitudinal Tracking (see Longitudinal Tracking). But there is no Longitudinal Tracking procedure. If it is the same as the Longitudinal Tracking, why aren't you just using that procedure?
- c) It also says "After terminal recording, the stimulation session will be performed (See Stimulation)." This final Non-Survival surgery should be part of the timeline in Q5 of the experiment. We need to know when this is happening. Is this the day after the Terminal recording? Does that mean the pig may be fasted two days in a row?

3) Within the Stimulation surgery, it says "3D deformational changes in the tongue base (SONO) and respiratory parameters (Pneumotach system) will be recorded along with stimulation pulses under x-ray videofluoroscopy." Is that in addition to the same procedures occurring just prior as part of the Terminal Recording procedure?

If you need clarification on these questions, you can call me (206-291-3058).

Regards, Michelle From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Monday, August 31, 2020 4:16 PM

To: Michelle Brot

Subject: Re: Still need some questions answered.....

Michelle,

Thank you for sending me these questions. Please see below for my answers:

1) Are the obese pigs in Aim 2 going to be fed a high fat diet while they are at UW? If so, the Special Diet procedure that you created needs to be added back into the list of procedures and this needs to be mentioned in Q5 of Exp 002. If not, the second sentence in the Q12 Husbandry exceptions for the Special/medicated Diet needs to be removed:

Pigs - Barium diet will be provided during each recording session. Ad lib feeding Special/medicated diet will be applied for obese minipigs with a high fat diet.

I added a new special diet :ad lib feeing with high fat diet in Aim 2 doe obese minipigs only. The vendors will feed the pigs to be obese and the same diet will be provided by the vendor during the entire experimental period.

2) In Aim 01, Q5, it says "Day 48: Terminal recording. *Please note that the terminal surgery may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal surgery.*" and there is the same sentence in Aim 2 for Day 57.

The terminal surgery has been changed to the terminal recording for the clarification.

a) Is the "terminal surgery" the same as the "Stimulation Surgery"? You need to refer to it in Q5 as you call it in the Procedure Name.

The two procedures are included in the terminal day, 1. terminal recording; and 2. stimulation.

b) When I read about the Terminal Recording procedure in "Behavioral Testing: Terminal Recording (w/Food Restriction)", it says that Terminal Recording is the same as Longitudinal Tracking (see Longitudinal Tracking). But there is no Longitudinal Tracking procedure. If it is the same as the Longitudinal Tracking, why aren't you just using that procedure?

The category has been changed to "other" as for the longitudinal tracking. Since there will be two different procedures in the terminal day as mentioned above, it would be better to name as "terminal recording".

c) It also says "After terminal recording, the stimulation session will be performed (See Stimulation)." This final Non-Survival surgery should be part of the timeline in Q5 of the experiment. We need to know when this is happening. Is this the day after the Terminal recording? Does that mean the pig may be fasted two days in a row?

As mentioned above, the two procedures will be in the same day. The timelines for both Aims have been revised.

3) Within the Stimulation surgery, it says "3D deformational changes in the tongue base (SONO) and respiratory parameters (Pneumotach system) will be recorded along with stimulation pulses under x-ray videofluoroscopy." Is that in addition to the same procedures occurring just prior as part of the Terminal Recording procedure?

The recording of x-ray videofluoroscopy in the stimulation session will be performed under anesthesia, but the prior x-ray videofluoroscopic recording will be in awakening status (barium diet feeding).

Hope these would be satisfactory,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, August 31, 2020 2:18 PM

To: Zi-Jun Liu <zjliu@uw.edu>

Subject: Still need some questions answered.....

Hi Zee,

The IACUC reviewer wanted me to check with you on a couple items:

1) Are the obese pigs in Aim 2 going to be fed a high fat diet while they are at UW? If so, the Special Diet procedure that you created needs to be added back into the list of procedures and this needs to be mentioned in Q5 of Exp 002. If not, the second sentence in the Q12 Husbandry exceptions for the Special/medicated Diet needs to be removed:

Pigs - Barium diet will be provided during each recording session. Ad lib feeding Special/medicated diet will be applied for obese minipigs with a high fat diet.

- 2) In Aim 01, Q5, it says "Day 48: Terminal recording. *Please note that the terminal surgery may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal surgery.*" and there is the same sentence in Aim 2 for Day 57.
- a) Is the "terminal surgery" the same as the "Stimulation Surgery"? You need to refer to it in Q5 as you call it in the Procedure Name.
- b) When I read about the Terminal Recording procedure in "Behavioral Testing: Terminal Recording (w/Food Restriction)", it says that Terminal Recording is the same as Longitudinal Tracking (see Longitudinal Tracking). But there is no Longitudinal Tracking procedure. If it is the same as the Longitudinal Tracking, why aren't you just using that procedure?
- c) It also says "After terminal recording, the stimulation session will be performed (See Stimulation)." This final Non-Survival surgery should be part of the timeline in Q5 of the experiment. We need to know when this is happening. Is this the day after the Terminal recording? Does that mean the pig

may be fasted two days in a row?

3) Within the Stimulation surgery, it says "3D deformational changes in the tongue base (SONO) and respiratory parameters (Pneumotach system) will be recorded along with stimulation pulses under x-ray videofluoroscopy." Is that in addition to the same procedures occurring just prior as part of the Terminal Recording procedure?

If you need clarification on these questions, you can call me (206-291-3058).

Regards, Michelle From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Friday, August 21, 2020 8:58 AM

To: Michelle Brot

Subject: Re: Timeline estimate

Michele,

Glad to know that the review process has moved forward. for the all timelines proposed, I would say "the timelines could vary up to 3 days".

Thank you,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Thursday, August 20, 2020 7:30 PM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Timeline estimate

Hi Zee,

I have moved your protocol into Committee Review so it should be approved a week from tomorrow (Aug. 28) as long as the Commitee doesn't have any questions.

However, in the meantime, the vet requested that you place some parameters around this general statement you put in that adds flexibility: "Please note that the following timelines are approximate, and subject to be modified upon the detailed situation." This is for the general timeline in Q5 for each experiment. Would you be able to tell me about how long you think the dates could vary, e.g., the timeline could vary "up to x days". I can add the information for you.

From: Michelle Brot <mbrot@uw.edu>
Sent: Friday, August 28, 2020 1:02 PM

To: Zi-Jun Liu

Subject: Re: Timeline estimate

Hi Zee,

It looks like the IACUC reviewer questions were sent out to you this morning. Please note that I already corrected the last one, which asks you to give an approximate timeframe for your procedures in each experiment (you had told me to add +/- 3 days), so you can say that was added.

Feel free to get in touch if you have trouble responding to any of the questions.

Regards, Michelle

From: Michelle Brot <mbrot@uw.edu> Sent: Thursday, August 27, 2020 1:45 PM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Re: Timeline estimate

Hi Zee,

I took a look at your protocol in Committee Review and saw that there are a number of questions from the Committee reviewer that you will need to address when it comes out tomorrow. I wanted to let you know so that you can make time to work on it. You'll probably get them around noon or early afternoon.

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From: Michelle Brot <mbrot@uw.edu>
Sent: Friday, August 21, 2020 9:01 AM

To: Zi-Jun Liu

Subject: Re: Timeline estimate

Very good, I'll add it....thanks, Zee!!

Take care, Michelle

From: Zi-Jun Liu <zjliu@uw.edu>
Sent: Friday, August 21, 2020 8:58 AM
To: Michelle Brot <mbrot@uw.edu>
Subject: Re: Timeline estimate

Michele,

Glad to know that the review process has moved forward. for the all timelines proposed, I would say "the timelines could vary up to 3 days".

Thank you,

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Thursday, August 20, 2020 7:30 PM

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From: Zi-Jun Liu <zjliu@uw.edu>

Sent: Friday, August 28, 2020 3:08 PM

To: Michelle Brot

Subject: Re: Timeline estimate

Michelle,

Thank you for the heads-up. I have done the revisions and sent the protocol back to the committee.

Zee

From: Michelle Brot <mbrot@uw.edu> Sent: Friday, August 28, 2020 1:02 PM

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Thanks, Michelle From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 17, 2020 8:56 AM

To: Molly K. Lucas

Subject: Re: Zee Liu pig protocol

Thanks, Molly. I know it was a lot of work to review Zee's responses. I will check in with the other reviewers at our next meeting about the issue you raised regarding having a time parameter included in general statements like Zee included.

Take care, Michelle

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Sunday, August 16, 2020 1:35 PM **To:** Michelle Brot <mbrot@uw.edu>

Subject: Zee Liu pig protocol

Hi Michelle,

I just turned around my 2nd vet consult. One thing I didn't put in Hoverboard but wanted to ask you to think about, is that in response to my recommendation to add some flexibility in timing in Q #5 of the experiments, he added, "Please note that the following timelines are approximate, and subject to be modified upon the detailed situation." I think this is an improvement, because sometimes things happen like the MRI isn't available, or a fasting mistake is made, and procedures have to be put off a day or two. I am thinking that there are often more specific parameters around this, though, esp in large animal protocols (e.g., I've seen some that say the timeline could vary but "up to x days").

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Thanks, Molly From: Molly K. Lucas <mklucas@uw.edu>
Sent: Tuesday, August 25, 2020 3:54 PM

To: Kim Stocking

Subject: Re: Zee Liu pig protocol

Hi Kim,

That all sounds reasonable to me, thanks for the updates.

Molly

From: Kim Stocking <kstock@uw.edu> Sent: Tuesday, August 25, 2020 3:25 PM To: Molly K. Lucas <mklucas@uw.edu> Subject: RE: Zee Liu pig protocol

Hi Molly-

This topic was discussed at a reviewer meeting and everyone agreed that we usually have specific parameters on potential variations to the timeline on USDA covered species protocols. I have added a comment (to include up to 3 days variation) to the protocol while it's in committee review. Otherwise, I didn't have any other specific questions/comments on this protocol.

Thea didn't advocate putting this protocol on vet monitoring unless there are issues that become apparent while vet services is there doing the anesthesia.

Kim

From: Molly K. Lucas <mklucas@uw.edu> Sent: Sunday, August 23, 2020 10:07 AM To: Kim Stocking <kstock@uw.edu> Subject: Fw: Zee Liu pig protocol

fyi - not sure if this has been discussed yet.

Molly

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Sent: Sunday, August 16, 2020 1:35 PM **To:** Michelle Brot <<u>mbrot@uw.edu</u>> **Subject:** Zee Liu pig protocol

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Thanks, Molly From:

Kim Stocking <kstock@uw.edu> Tuesday, August 25, 2020 3:26 PM

Sent: To:

Molly K. Lucas

Subject:

RE: Zee Liu pig protocol

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Thanks, Molly From: Molly K. Lucas <mklucas@uw.edu>
Sent: Monday, August 17, 2020 9:39 AM

To: Nicholas L. Reyes

Subject: Re: Zee Liu protocol - revision

Hi Nick,

I submitted the vet consult yesterday with this question:

"Other: Liu-Minipig: Catheter and Wire Electrode (Team) and Other: Liu-Minipig: Baseline recording, ver. 1 (Team):

Please edit to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure exactly where the sutures might be placed and whether re-sedation/anesthesia will be needed for removal?)."

It does sound like the pig might be groggy (awake enough to have eaten though). That sounds like a good idea re: the local. It looks like he's actually working on it right now (a different Q from yesterday has a response) - I'll let you know what he says.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Monday, August 17, 2020 9:31 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: Zee Liu protocol - revision

I'm guessing that he just plans to pull the red rubber (and remove the sutures?) on the awake pig. This may be possible if the pig is eating or still groggy from the procedure. Unfortunately I can't remember how this worked previously. We could recommend using tape instead of sutures but probably wouldn't hold effectively and might be just as annoying to remove from the pig while its awake. I would probably be okay with the sutures but maybe we should ask hi top administer a little local at the suture sites so its not painful to remove them?

Nick

From: Molly K. Lucas <mklucas@uw.edu> Sent: Sunday, August 16, 2020 11:57 AM To: Nicholas L. Reyes <nlreyes@uw.edu> Subject: Re: Zee Liu protocol - revision

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Molly

Under light anesthesia, insertion of a pair of wire electrodes (0.1mm) into the right middle pharyngeal constrictor muscle and the placement of a face mask connecting with pneumotach sensor. After a few minutes recording of x-ray videofluoroscopy, replacement of the face mask by a #10 French red rubber catheter inserted into the right nasal cavity 3-5cm deep and secured to nearby nasal skin by suturing, and placements of chest/abdominal belts and oximeter ear clip. Catheter, EMG leads, belts, and oximeter will be connected to a BioRadio receiver box in the back pocket of the jacket.

After waking up, the videofluoroscopic swallowing examination (VFSE) will be performed for respiration and voluntary swallowing during unrestrained feeding. After 10-15' of feeding on the barium diet, sensors and wire electrodes will be removed, and the pig will return to its pen.

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Thursday, August 13, 2020 9:06 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: Zee Liu protocol - revision

Hi Molly,

Glad to hear that the red rubber catheter does not appear to be a replacement of the mask iso. ..not confident they will get it to work but I am okay with them including it in thier plans. Maybe a clarification in regards to how it will be secured (tape vs. suture vs some other means) would be good. Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 12, 2020 4:48 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Subject: Zee Liu protocol - revision

Hi Nick,

The revision is back in my inbox. So far I've read the responses to my questions, which overall look promising (e.g., no re-implantation except at terminal surgery). I still need to go through and verify that all of the changes were made and with sufficient detail, etc. but so far, so good.

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To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/18/2020 12:37:35 PM

Subject: Re: Zee Liu protocol - revision

Hi Nick,

Another revision is back to me. Here's what he said about the catheter (below). fyi, I think I am almost done with it. This time I just edited the response about the surgeon/animal prep for the surgeries and asked one final question, which is how the masseter muscle is approached during the tongue reduction surgery - from the surgery description I can't tell if it's from the outside (skin incision) vs. the inside (inner cheek).

If you want to look at anything there will still be time (it will go to the committee next) to ask any questions. I asked to see it back to see the response about the approach, but I hope not to have any additional comments/questions.

Thanks for your help with this. It was a lot of work.

Molly

Other: Liu-Minipig: Catheter and Wire Electrode (Team) and Other: Liu-Minipig: Baseline recording, ver. 1 (Team):

Please edit to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure exactly where the sutures might be placed and whether re-sedation/anesthesia will be needed for removal?).

Change Request Completed - Zi-Jun Liu - 8/17/2020 10:05 AM The removal of the catheter will be the same as we did in the live sleep monitoring in minipigs.

Same as the previously applied, the suture will be in the nearby skin around the nose.

The revisions have been done accordingly, including in the procedure section.

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Monday, August 17, 2020 9:31 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: Zee Liu protocol - revision

I'm guessing that he just plans to pull the red rubber (and remove the sutures?) on the awake pig. This may be possible if the pig is eating or still groggy from the procedure. Unfortunately I can't remember how this worked previously. We could recommend using tape instead of sutures but probably wouldn't

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Nick

From: Molly K. Lucas <mklucas@uw.edu> Sent: Sunday, August 16, 2020 11:57 AM To: Nicholas L. Reyes <nlreyes@uw.edu> Subject: Re: Zee Liu protocol - revision

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If you understand it though, let me know ©

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From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Thursday, August 13, 2020 9:06 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: Zee Liu protocol - revision

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Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu
206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 12, 2020 4:48 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Subject: Zee Liu protocol - revision

Hi Nick,

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Thanks, Molly

Veterinarian Change Request (response required)
Jump To: Experiments
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From: Molly K. Lucas <mklucas@uw.edu>
Sent: Tuesday, August 18, 2020 12:38 PM

To: Nicholas L. Reyes

Subject: Re: Zee Liu protocol - revision

Hi Nick,

Another revision is back to me. Here's what he said about the catheter (below). fyi, I think I am almost done with it. This time I just edited the response about the surgeon/animal prep for the surgeries and asked one final question, which is how the masseter muscle is approached during the tongue reduction surgery - from the surgery description I can't tell if it's from the outside (skin incision) vs. the inside (inner cheek).

If you want to look at anything there will still be time (it will go to the committee next) to ask any questions. I asked to see it back to see the response about the approach, but I hope not to have any additional comments/questions.

Thanks for your help with this. It was a lot of work.

Molly

Other: Liu-Minipig: Catheter and Wire Electrode (Team) and Other: Liu-Minipig: Baseline recording, ver. 1 (Team):

Please edit to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure exactly where the sutures might be placed and whether re-sedation/anesthesia will be needed for removal?).

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From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/17/2020 9:38:35 AM

Subject: Re: Zee Liu protocol - revision

Hi Nick,

I submitted the vet consult yesterday with this question:

"Other: Liu-Minipig: Catheter and Wire Electrode (Team) and Other: Liu-Minipig: Baseline recording, ver. 1 (Team):

Please edit to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure exactly where the sutures might be placed and whether re-sedation/anesthesia will be needed for removal?)."

It does sound like the pig might be groggy (awake enough to have eaten though). That sounds like a good idea re: the local. It looks like he's actually working on it right now (a different Q from yesterday has a response) - I'll let you know what he says.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Monday, August 17, 2020 9:31 AM To: Molly K. Lucas <mklucas@uw.edu> Subject: Re: Zee Liu protocol - revision

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To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/16/2020 11:57:07 AM

Subject: Re: Zee Liu protocol - revision

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From: Nicholas L. Reyes <nlreyes@uw.edu>

Sent: Monday, July 27, 2020 4:30 PM

To: Molly K. Lucas
Cc: Kim Stocking

Subject: Re: Zee pig protocol

Excellent. I will put some pressure on him to get a meeting together if he doesn't respond to this follow-up email.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 4:28 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu> Subject: Re: Zee pig protocol

Hi Nick,

That sounds great to me - I'd much rather not try to review it until you've had a chance to work through the anesthesia plan and those changes are incorporated. I agree that plan seems much more efficient. I'll enter a comment to meet with VS and make any edits and resubmit, that way it's not sitting in vet consult and the message is clear that the meeting is the first step of the vet consult process.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Monday, July 27, 2020 4:21 PM To: Molly K. Lucas <mklucas@uw.edu> Cc: Kim Stocking <kstock@uw.edu>

Subject: Re: Zee pig protocol

Hey Molly,

Zi actually reached out to VSreview on the 21st for a review of the anesthesia for this project. I had Alex email back to set up a meeting for us to all get together and come up with an anesthesia plan (me, Gary and the anesthesia resident). I think that tends to work much better with him than trying to dig into his descriptions and go back and forth. I'd like to try to get a chance to meet with him before going too critically into his descriptions because I think the plan is likely to change after we meet.

Unfortunately, he has not responded to our email. I am asking Alex to reach out again and include me so that I can urge him to meet with us soon if possible. Do you think this is doable or should we just review as is written.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 3:49 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu>

Subject: Zee pig protocol

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Thanks, Molly From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, July 27, 2020 5:16 PM
To: Molly K. Lucas; Kim Stocking

Subject: Re: Zee pig protocol

Thanks for the update and rapid processing of the protocol, Molly. It's likely to be a bit challenging so I'm glad Nick, et al will be able to do their review first to ease the way for you. Let me know if there's anything I can do to help as Zee and I have a close working relationship these days ©.

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 4:32 PM To: Michelle Brot <mbrot@uw.edu> Subject: Fw: Zee pig protocol

fyi

Molly

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Zi-Liu has received a grant and has resurrected his minipig protocol. Please prioritize this as the funding agency is waiting for its approval. Nick is very familiar with Zee's procedures and also, Zee e-mailed Gary Fye and asked him to review the Anesthesia procedure description to make sure it sounds consistent with what Vet Services does.

Maybe we can both go through it and compare notes?

Thanks, Molly From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, July 27, 2020 5:16 PM
To: Molly K. Lucas; Kim Stocking

Subject: Re: Zee pig protocol

Thanks for the update and rapid processing of the protocol, Molly. It's likely to be a bit challenging so I'm glad Nick, et al will be able to do their review first to ease the way for you. Let me know if there's anything I can do to help as Zee and I have a close working relationship these days ©.

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 4:32 PM To: Michelle Brot <mbrot@uw.edu> Subject: Fw: Zee pig protocol

fyi

Molly

From: Molly K. Lucas <mklucas@uw.edu>
Sent: Monday, July 27, 2020 4:28 PM

To: Nicholas L. Reyes <nlreyes@uw.edu>
Cc: Kim Stocking <kstock@uw.edu>

Subject: Re: Zee pig protocol

Hi Nick,

That sounds great to me - I'd much rather not try to review it until you've had a chance to work through the anesthesia plan and those changes are incorporated. I agree that plan seems much more efficient. I'll enter a comment to meet with VS and make any edits and resubmit, that way it's not sitting in vet consult and the message is clear that the meeting is the first step of the vet consult process.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Monday, July 27, 2020 4:21 PM To: Molly K. Lucas <mklucas@uw.edu>

Cc: Kim Stocking <kstock@uw.edu>
Subject: Re: Zee pig protocol

Hey Molly,

Zi actually reached out to VSreview on the 21st for a review of the anesthesia for this project. I had Alex email back to set up a meeting for us to all get together and come up with an anesthesia plan (me, Gary and the anesthesia resident). I think that tends to work much better with him than trying to dig

into his descriptions and go back and forth. I'd like to try to get a chance to meet with him before going too critically into his descriptions because I think the plan is likely to change after we meet. Unfortunately, he has not responded to our email. I am asking Alex to reach out again and include me so that I can urge him to meet with us soon if possible. Do you think this is doable or should we just review as is written.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Molly K. Lucas <mklucas@uw.edu> Sent: Monday, July 27, 2020 3:49 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Kim Stocking <kstock@uw.edu>

Subject: Zee pig protocol

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Maybe we can both go through it and compare notes?

Thanks, Molly

Nicholas L. Reyes <nlreyes@uw.edu> From: Sent: Thursday, August 6, 2020 8:37 AM

To: Molly K. Lucas **Subject:** Re: Zee protocol Q

Works for me. I'll take a look and we can discuss at 2.

Nick

From: Molly K. Lucas <mklucas@uw.edu> Sent: Thursday, August 6, 2020 8:34 AM To: Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Hi Nick,

Does 2pm work? I can do anytime between 2-5.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Thursday, August 6, 2020 8:33 AM To: Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Hey Molly,

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Nicholas Reves DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Thursday, August 6, 2020 6:55 AM To: Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

RCW 42.56.250(4)

Happy to discuss. I'm working from home tomorrow too. Feel free to call me on my cell

Nick

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 4:19 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

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To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

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Get Outlook for iOS

From: Michelle Brot <mbrot@uw.edu>

Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q RCW 42.56.070(1)

Thanks, Molly....I'll check on Surgery Certification for the pig surgery.

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 3:47 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu> **Cc:** Michelle Brot <mbrot@uw.edu>

Subject: Zee protocol Q

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FERPA

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| Daniel F Leotta | |
| Zi-Jun Liu | |
| Katherine Rafferty | |
| Vet Services | |
| Jeffrey Thiel | |
| [X] | |

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| Katherine Rafferty |
| Vet Services |
| Jeffrey Thiel |
| [X] |

From: Molly K. Lucas <mklucas@uw.edu>
Sent: Thursday, August 6, 2020 8:35 AM

To: Nicholas L. Reyes
Subject: Re: Zee protocol Q

Hi Nick,

I was actually drafting this when I got your email re: timing.

Some initial things to mull over - right now the surgeries don't include an analgesic plan, so I'm thinking we should suggest one. Not sure if you talked about that with him at all or if you were just focused on anesthesia? Also I've been mulling over the feeding plan. As written, they will be eating at limited times for many days in a row. They say they will get the regular amount of calories, and will be weighed weekly. I'm thinking maybe they should not get *too* much food at once (possible regurg, etc.). And since they are Yucatans they might be less willing to adapt to an unusual feeding schedule?

If I finish my draft questions (a Word doc) soon I'll send it to you so you can look them over before we talk.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 6:55 AM **To:** Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Happy to discuss. I'm working from home tomorrow too. Feel free to call me on my cell

RCW 42.56.250(4)

Nick

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 4:19 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Thanks Nick.

So I already have a pretty long list of questions for the vet consult and I'm only partway through. Some of them are just inconsistencies/cleanup/flexibility things, but I'm thinking it might be helpful to bounce a few other things off of you by phone, maybe sometime tomorrow ifg you have some time? I'm not ready today as I'm still working my way through it.

I'm free all afternoon tomorrow and I'll be working from home so on my cell.

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FERPA

RCW 42.56.070(1)

Sue Herring

NIRANJAN BALU

| Daniel F Leotta |
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| Zi-Jun Liu |
| Katherine Rafferty |
| Vet Services |
| Jeffrey Thiel |
| [X] |

From: Michelle Brot <mbr/>brot@uw.edu>
Sent: Wednesday, August 5, 2020 6:16 PM
To: Molly K. Lucas; Nicholas L. Reyes

Subject: Re: Zee protocol Q

Hi Molly,

Sure, I completely understand and I expected you to have numerous questions, and it may well require a couple rounds to get them answered. That being said, Zee is making good progress on using Hoverboard, which was part of my goal so I don't have to make all the edits for him!!

Thanks for working hard on this! ~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 5, 2020 4:32 PM

To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Sounds good Michelle, thanks. Just to warn you I'm only partway through and I already have quite a few questions... I know there's some time pressure re: granting agency but it needs some work...

Molly

From: Michelle Brot <mbrot@uw.edu>
Sent: Wednesday, August 5, 2020 4:26 PM
To: Nicholas L. Reyes <nlreyes@uw.edu>
Cc: Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Great. Thanks for the confirmation Nick. I can make that change to the Personnel page Molly.

On Aug 5, 2020, at 4:10 PM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

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RCW 42.56.250(4)

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| From: | Michelle Brot <mbrot@เ< th=""><th></th><th></th></mbrot@เ<> | | |
|---|---|---|---|
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| [X] |

Daniel F Leotta

From: Molly K. Lucas <mklucas@uw.edu>
Sent: Wednesday, August 5, 2020 4:20 PM

To: Nicholas L. Reyes
Subject: Re: Zee protocol Q

Thanks Nick.

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I'm free all afternoon tomorrow and I'll be working from home so on my cell.

Thanks, Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Wednesday, August 5, 2020 4:09 PM

To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Yes. Definitely. They do not have anyone in the group certified (or eligible to be certified) for pig anesthesia. Especially considering the addition of the attachment a doc- this should read that only vs will run anesthesia. Thanks for catching that!

Nicm

Get Outlook for iOS

From: Michelle Brot <mbrot@uw.edu>
Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

RCW 42.56.070(1)

Thanks, Molly....I'll check on Surgery Certification for the pig surgery.

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 3:47 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu> **Cc:** Michelle Brot <mbrot@uw.edu>

Subject: Zee protocol Q

Hi Nick,

I'm doing the vet consult now and just wanted to double check a few things with you.

FERPA

| Michelle has asked twice re: the personnel assigned to surgery and anesthesia. I think the surgery list looks OK as everyone on it appears to be certified (although Michelle, I don't actually see a certification entry for just that Part 1B and Part 2 were waived? Everyone else listed for surgery has the cert entry, can you check in that please?). | | | |
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| Vet Services | | | |
| Jeffrey Thiel | | | |
| [X] [X] [X] [X] [X] [X] | | | |
| [X] | | | |

| From: Sent: To: Subject: | Michelle Brot <mbrot@uw.edu> Wednesday, August 5, 2020 4:03 PM Molly K. Lucas; Nicholas L. Reyes Re: Zee protocol Q</mbrot@uw.edu> | |
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- [X]
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FERPA

From: Molly K. Lucas <mklucas@uw.edu>
Sent: Wednesday, August 5, 2020 4:32 PM
To: Michelle Brot; Nicholas L. Reyes

RCW 42.56.070(1)

Subject: Re: Zee protocol Q

Sounds good Michelle, thanks. Just to warn you I'm only partway through and I already have quite a few questions... I know there's some time pressure re: granting agency but it needs some work...

Molly

From: Michelle Brot <mbrot@uw.edu>
Sent: Wednesday, August 5, 2020 4:26 PM
To: Nicholas L. Reyes <nlreyes@uw.edu>
Cc: Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Great. Thanks for the confirmation Nick. I can make that change to the Personnel page Molly.

On Aug 5, 2020, at 4:10 PM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

Yes. Definitely. They do not have anyone in the group certified (or eligible to be certified) for pig anesthesia. Especially considering the addition of the attachment a doc- this should read that only vs will run anesthesia. Thanks for catching that!

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From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 9:00:21 AM **Subject:** Re: Zee protocol Q

Attach: [Liu Z 8 5 20.docx]

Sounds great. Here's what I have so far, and these are all for the Experiments page. The yellow highlight means it's a new question/comment. I tried to highlight things I specifically want to get your input on in green.

I am going to move on and look at Charlotte's protocol for our seminar, since I've been distracted by other protocols, and put this on the back burner until this afternoon when we talk.

Molly

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Subject: Re: Zee protocol Q

Works for me. I'll take a look and we can discuss at 2.

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Subject: Re: Zee protocol Q

Hey Molly,

I picked up a couple of additional meetings today but I want to make sure I am available to discuss this Liu stuff. Is there a time this afternoon that would work best for you?

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Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian

Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 6:55 AM **To:** Molly K. Lucas <mklucas@uw.edu>

RCW 42.56.250(4)

Subject: Re: Zee protocol Q

Happy to discuss. I'm working from home tomorrow too. Feel free to call me on my cell

Nick

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Q #3 at the bottom of the page: Re: the statement, "The interval between the two surgeries is 11 days." I recommend editing for a bit more flexibility just in case something happens and the interval is slightly different. It would be fine to say something like "at least 10 days."

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Attachments: Liu Z 8 5 20.docx

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RCW 42.56.250(4)

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FERPA RCW 42.56.070(1)

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From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 8:34:56 AM Subject: Re: Zee protocol Q

Hi Nick,

I was actually drafting this when I got your email re: timing.

Some initial things to mull over - right now the surgeries don't include an analgesic plan, so I'm thinking we should suggest one. Not sure if you talked about that with him at all or if you were just focused on anesthesia? Also I've been mulling over the feeding plan. As written, they will be eating at limited times for many days in a row. They say they will get the regular amount of calories, and will be weighed weekly. I'm thinking maybe they should not get *too* much food at once (possible regurg, etc.). And since they are Yucatans they might be less willing to adapt to an unusual feeding schedule?

If I finish my draft questions (a Word doc) soon I'll send it to you so you can look them over before we talk.

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To: Nicholas L. Reyes <nlreyes@uw.edu> **Subject:** Re: Zee protocol Q

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So I already have a pretty long list of questions for the vet consult and I'm only partway through. Some of them are just inconsistencies/cleanup/flexibility things, but I'm thinking it might be helpful to bounce a few other things off of you by phone, maybe sometime tomorrow ifg you have some time? I'm not ready today as I'm still working my way through it.

I'm free all afternoon tomorrow and I'll be working from home so on my cell.

Thanks, Molly

FERPA

RCW 42.56.070(1)

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Wednesday, August 5, 2020 4:09 PM

To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Yes. Definitely. They do not have anyone in the group certified (or eligible to be certified) for pig anesthesia. Especially considering the addition of the attachment a doc- this should read that only vs will run anesthesia. Thanks for catching that!

Nicm

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From: Michelle Brot <mbrot@uw.edu>

Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Thanks, Molly....I'll check on Surgery Certification for the pig surgery.

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 3:47 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu> **Cc:** Michelle Brot <mbrot@uw.edu>

Subject: Zee protocol Q

Hi Nick,

I'm doing the vet consult now and just wanted to double check a few things with you.

Michelle has asked twice re: the personnel assigned to surgery and anesthesia. I think the surgery list looks OK as everyone on it appears to be certified (although Michelle, I don't actually see a certification entry for just that Part 1B and Part 2 were waived? Everyone else listed for surgery has the cert entry, can you check in that please?).

However, the anesthesia personnel are pasted below. I am thinking it should only be vet services listed, does that sound correct to you?

Molly

NIRANJAN BALU

Sue Herring

Daniel F Leotta

Zi-Jun Liu

Katherine Rafferty

Vet Services

Jeffrey Thiel

From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/6/2020 8:34:03 AM Subject: Re: Zee protocol Q

Hi Nick,

Does 2pm work? I can do anytime between 2-5.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 8:33 AM **To:** Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Hey Molly,

I picked up a couple of additional meetings today but I want to make sure I am available to discuss this Liu stuff. Is there a time this afternoon that would work best for you?

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Thursday, August 6, 2020 6:55 AM **To:** Molly K. Lucas <mklucas@uw.edu>

: Molly K. Lucas <mklucas@uw.edu> RCW 42.56.250(4)

Subject: Re: Zee protocol Q

Happy to discuss. I'm working from home tomorrow too. Feel free to call me on my cell

Nick

Frame Mally V Lucas webbers @www.adva

From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Wednesday, August 5, 2020 4:19 PM **To:** Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Thanks Nick.

So I already have a pretty long list of questions for the vet consult and I'm only partway through. Some of them are just inconsistencies/cleanup/flexibility things, but I'm thinking it might be helpful to

bounce a few other things off of you by phone, maybe sometime tomorrow ifg you have some time? I'm not ready today as I'm still working my way through it.

I'm free all afternoon tomorrow and I'll be working from home so on my cell.

Thanks, Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Wednesday, August 5, 2020 4:09 PM

To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Yes. Definitely. They do not have anyone in the group certified (or eligible to be certified) for pig anesthesia. Especially considering the addition of the attachment a doc- this should read that only vs will run anesthesia. Thanks for catching that!

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From: Michelle Brot <mbrot@uw.edu>

Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q RCW 42.56.070(1)

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~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 5, 2020 3:47 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Michelle Brot <mbrot@uw.edu>

Subject: Zee protocol Q

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I'm doing the vet consult now and just wanted to double check a few things with you.

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FERPA

FERPA RCW 42.56.070(1)

NIRANJAN BALU

Sue Herring

Daniel F Leotta

Zi-Jun Liu

Katherine Rafferty

Vet Services

Jeffrey Thiel

From: Michelle Brot <mbrot@uw.edu>

To: "Molly K. Lucas" <mklucas@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/5/2020 6:15:58 PM **Subject:** Re: Zee protocol Q

Hi Molly,

Sure, I completely understand and I expected you to have numerous questions, and it may well require a couple rounds to get them answered. That being said, Zee is making good progress on using Hoverboard, which was part of my goal so I don't have to make all the edits for him!!

Thanks for working hard on this!

~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 5, 2020 4:32 PM

To: Michelle Brot <mbrot@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

Sounds good Michelle, thanks. Just to warn you I'm only partway through and I already have quite a few questions... I know there's some time pressure re: granting agency but it needs some work...

Molly

From: Michelle Brot <mbrot@uw.edu>
Sent: Wednesday, August 5, 2020 4:26 PM
To: Nicholas L. Reyes <nlreyes@uw.edu>
Cc: Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

Great. Thanks for the confirmation Nick. I can make that change to the Personnel page Molly.

On Aug 5, 2020, at 4:10 PM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

Yes. Definitely. They do not have anyone in the group certified (or eligible to be certified) for pig anesthesia. Especially considering the addition of the attachment a doc- this should read that only vs will run anesthesia. Thanks for catching that!

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Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

FERPA

RCW 42.56.070(1)

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To: Nicholas L. Reyes <nlreyes@uw.edu>
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Katherine Rafferty

Vet Services

Jeffrey Thiel

From: "Molly K. Lucas" <mklucas@uw.edu>

To: Michelle Brot <mbrot@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/5/2020 4:32:08 PM Subject: Re: Zee protocol Q

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Sent: Wednesday, August 5, 2020 4:26 PM
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Sent: Wednesday, August 5, 2020 4:03:15 PM

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Zi-Jun Liu

Katherine Rafferty

Vet Services

Jeffrey Thiel

Obtained by Rise for Animals. Uploaded to Animal Research Laboratory Overview (ARLO) on 05/13/2021

From: Michelle Brot <mbrot@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>
CC: "Molly K. Lucas" <mklucas@uw.edu>

Sent: 8/5/2020 4:26:12 PM Subject: Re: Zee protocol Q

Great. Thanks for the confirmation Nick. I can make that change to the Personnel page Molly.

On Aug 5, 2020, at 4:10 PM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

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Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

RCW 42.56.070(1)

FERPA

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| Katherine Rafferty |
|--------------------|
| Vet Services |
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Daniel F Leotta

Zi-Jun Liu

From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/5/2020 4:19:41 PM Subject: Re: Zee protocol Q

Thanks Nick.

So I already have a pretty long list of questions for the vet consult and I'm only partway through. Some of them are just inconsistencies/cleanup/flexibility things, but I'm thinking it might be helpful to bounce a few other things off of you by phone, maybe sometime tomorrow ifg you have some time? I'm not ready today as I'm still working my way through it.

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From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Wednesday, August 5, 2020 4:09 PM

To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zee protocol Q

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Sent: Wednesday, August 5, 2020 4:03:15 PM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zee protocol Q

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| Molly | | | | | | | |
| FERPA | | | | | | | |
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| | | | | | | | |

FERPA RCW 42.56.070(1)

Sent: 8/5/2020 4:03:15 PM Subject: Re: Zee protocol Q Thanks, Molly....I'll check on Surgery Certification for the pig surgery. ~Michelle From: Molly K. Lucas <mklucas@uw.edu> Sent: Wednesday, August 5, 2020 3:47 PM To: Nicholas L. Reyes <nlreyes@uw.edu> Cc: Michelle Brot <mbrot@uw.edu> Subject: Zee protocol Q Hi Nick, I'm doing the vet consult now and just wanted to double check a few things with you. Michelle has asked twice re: the personnel assigned to surgery and anesthesia. I think the surgery list looks OK as everyone on it appears to be certified (although Michelle, I don't actually see a certification entry for just that Part 1B and Part 2 were waived? Everyone else listed for surgery has the cert entry, can you check in that please?). However, the anesthesia personnel are pasted below. I am thinking it should only be vet services listed, does that sound correct to you? Molly **NIRANJAN BALU** Sue Herring Daniel F Leotta Zi-Jun Liu **Katherine Rafferty Vet Services** Jeffrey Thiel

To: "Molly K. Lucas" <mklucas@uw.edu>, "Nicholas L. Reyes" <nlreyes@uw.edu>

From: Michelle Brot <mbrot@uw.edu>

From: Nicholas L. Reyes <nlreyes@uw.edu>
Sent: Tuesday, August 4, 2020 10:56 AM

Aliah alla Brate Malle K Leasa

To: Michelle Brot; Molly K. Lucas

Subject: Re: Zi-Liu protocol

By the way Michelle, would you still like me to provide this to Zee for his protocol or should I just let him know that you will add this anesthetic plan to the AUP as a new procedure.

Thanks again,

Nick

Nicholas Reyes DVM, MS, DACLAM
Sr. Staff Veterinarian
Co-Director of Animal Facility Operations
Dept. of Comparative Medicine
University of Washington, Seattle
nlreyes@uw.edu
206-543-0267

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Tuesday, August 4, 2020 10:52 AM

To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

Subject: Re: Zi-Liu protocol

Excellent. I agree that this would be the best way. I have attached the current version of this doc for reference. The only question I have would be in the case that we update the doc (add drugs), is there a way to update it across the protocols which include the procedure without reviewing it for each or would we risk having different versions in different protocols? I don't foresee major changes soon, but we have updated it twice already since it was initially drafted 4-5 years ago.

Thanks, Nick

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Dept. of Comparative Medicine
University of Washington, Seattle
nlreyes@uw.edu
206-543-0267

From: Michelle Brot <mbrot@uw.edu> Sent: Tuesday, August 4, 2020 10:43 AM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Molly and Nick,

I agree that as long as it's in there and is consistent with Vet Services' practices, it is simplest to continue with what a lot of groups do, which is a simple procedure called "

<u>Vet Services Administered Anesthestics</u>" which refers to an attachment at the end of the procedure that lists all potential anesthetics that may be used in a surgery or other procedure for that species. Here is what it says in Herring's Q2 "**Describe step-by-step the procedure for administering the substance(s):** " for the anesthetics administration procedure "Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended."

The way Nick described the paramedic protocol with individual entries for each agent sounds like overkill and I'm not sure why that was set up that way.

Thanks! ~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Tuesday, August 4, 2020 9:54 AM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Michelle can you weigh in on this? I personally don't have an opinion re: how the information is presented as long as it's in there.

Molly

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To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Thanks Molly,

The reason I ask is that I met with the paramedic lab group last week and they had a protocol question. In looking at their anesthesia section I saw that they had each drug added in individually (maybe transcribed from the attachment). Seemed like a lot of work to get input and potentially some chance for error in transcribing... that's why I thought I would check before I continue handing it off to investigators.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

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From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Tuesday, August 4, 2020 9:48:38 AM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Nick and Michelle,

I know there are plenty of large animal protocols that have the attachment, so unless something has changed in OAW, I think it's fine to do that (there's definitely a precedent).

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Tuesday, August 4, 2020 9:03 AM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

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nlreyes@uw.edu
206-543-0267

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From: Molly K. Lucas <mklucas@uw.edu>
Sent: Saturday, August 1, 2020 3:31:17 PM
To: Michelle Brot <mbrot@uw.edu>
Cc: Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Michelle,

I'm cc'ing Nick so he can let us know if Zee will be making any edits to anesthesia (or anything else) as a

result of the meeting.

I was hoping edits could happen prior to it coming back to vet consult, and then hopefully the vet consult will be smoother. I believe it does still need a review (I have not yet looked at it closely).

Molly

From: Michelle Brot <mbrot@uw.edu> Sent: Friday, July 31, 2020 2:48 PM To: Molly K. Lucas <mklucas@uw.edu>

Subject: Zi-Liu protocol

Hi Molly,

I see that you're out of the office today. I just wanted to check in with you to see if you will need me to send Zee's protocol to Vet Consult again for you to review it since it's currently in Pre-Review. I don't see any indication that changes were made after their Vet Services meeting about the anesthesia plan yesterday so I'm just touching base in case you have any more information. Hope you are enjoying your time away and we can connect next week.

Take care, Michelle

Nicholas L. Reyes <nlreyes@uw.edu> From: Sent: Tuesday, August 4, 2020 10:53 AM

To: Michelle Brot; Molly K. Lucas

Subject: Re: Zi-Liu protocol

Attachments: Attachment A-MANUAL OF STANDARD OPERATING PROCEDURES.NR edit

12.14.18.docx

Excellent. I agree that this would be the best way. I have attached the current version of this doc for reference. The only question I have would be in the case that we update the doc (add drugs), is there a way to update it across the protocols which include the procedure without reviewing it for each or would we risk having different versions in different protocols? I don't foresee major changes soon, but we have updated it twice already since it was initially drafted 4-5 years ago.

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Subject: Re: Zi-Liu protocol

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I'm cc'ing Nick so he can let us know if Zee will be making any edits to anesthesia (or anything else) as a result of the meeting.

I was hoping edits could happen prior to it coming back to vet consult, and then hopefully the vet consult will be smoother. I believe it does still need a review (I have not yet looked at it closely).

Molly

From: Michelle Brot <mbrot@uw.edu> **Sent:** Friday, July 31, 2020 2:48 PM **To:** Molly K. Lucas <mklucas@uw.edu>

Subject: Zi-Liu protocol

Hi Molly,

I see that you're out of the office today. I just wanted to check in with you to see if you will need me to send Zee's protocol to Vet Consult again for you to review it since it's currently in Pre-Review. I don't see any indication that changes were made after their Vet Services meeting about the anesthesia plan yesterday so I'm just touching base in case you have any more information. Hope you are

| enjoying your time away and we can connect next week. | | | | | | | |
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| Take care, Michelle | | | | | | | |
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Attachment A

MANUAL OF STANDARD OPERATING PROCEDURES

Anesthesia/Analgesia of the Pig

University of Washington

Center for Videoendoscopic Surgery

Seattle, WA, 98195-6410

I. Introduction/Purpose

A. The purpose of this SOP is to provide appropriate dose ranges for a variety of anesthetic and analgesic drug options which may be utilized by Vet Services staff for the induction and maintenance of anesthesia in pigs.

II. Procedures

- A. General: The CVES animal lab is administered by the Department of Surgery to provide accredited animal surgical care for training and research animals. The Director of CVES is the faculty member in charge.
- B. The following anesthetic drug regimen is the most common protocol used by CVES:
 - 1. Preanesthesia: Glycopyrrolate .01 mg/kg
 - 2. Induction: Telazol 1-5.5 mg/kg I.M.; Xylazine 1-5.5 mg/kg I.M.
 - 3. Maintenance: Isoflurane 1% 3%
- C. Other drug dosages used for anesthesia/analgesia in pig:

1. Preanesthetics:

- a. Glycopyrrolate .01 mg/kg
- b. Atropine .02-.05 mg/kg I.M. Atropine is injected 10-15 minutes before endotracheal intubation to dry bronchial secretions and prevent bradycardia due to vagal stimulation.
- c. Diazepam 2 mg/kg I.M. Best when used in combination with Ketamine.
- d. Diazepam 2 mg/kg I.M.: Ketamine 10 mg/kg I.M.
- e. Acepromazine 0.2 mg/kg I.M. May produce hypotension and bradycardia. Do not give more than 15 mg/pig.
- f. Droperidol 2 mg/kg I.V., 4 mg/kg I.M.
- g. Ketamine 20-33 mg/kg I.M.
- h. Butorphanol 0.1-0.3mg/kg: Xylazine 1-4mg/kg I.M.
- i. Midazolam 0.1-0.5mg/kg (can be used alone as premedication sedation or in combination with butorphanol and/or xylazine as doses listed in h.)

2. Dissociative agents and combinations:

a. Ketamine 11-33 mg/kg I.M., I.V. Increases intracranial pressure. Poor muscle relaxation.

Increases heart rate and blood pressure and decreases

- cardiac contractility. Use with caution in animals with hepatic and renal disease.
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- c. Ketamine 15 mg/kg: Diazepam 2 mg/kg I.M.
- d. Ketamine 20 mg/kg: Xylazine 2 mg/kg I.M.
- e. Ketamine 11 mg/kg: Fentanyl-Droperidol 1mL/14kg I.M.
- f. Ketamine 15 mg/kg: Azaperone 2 mg/kg I.M.
- g. Ketamine 2 mg/kg: Xylazine 2 mg/kg: Oxymorphone .075 mg/kg I.V. (2x dose for I.M.)
- h. Ketamine 20 mg/kg: Climazolam .5-1.0 mg/kg I.M.
- i. Tiletamine-Zolazepam (Telazol) 4-6 mg/kg I.M.
- j. Tiletamine-Zolazepam (Telazol) 4-6 mg/kg: Xylazine 2.2 mg/kg I.M.
- k. "G-K-X": 5% guaifenesin-0.1% ketamine-0.1%xylazine in 5% dextrose solution: 1mg ketamine, 1mg xylazine and 50mg guaifenesen per mL of 5% dextrose solution.
 - i. G-K-X induction bolus: 1 ml/kg I.V.
 - ii. G-K-X maintenance infusion: 1-4ml/kg/hr I.V.

3. Barbiturates:

- a. Pentobarbital 20-40 mg/kg I.V.; 5-15 mg/kg/hr continuous I.V. infusion. May cause some respiratory depression and sedation, and may induce histamine release resulting in peripheral vasodialation. May delay gastric emptying, increase intestinal peristalsis and cause spasm of biliary tract.
- b. Thiopental 6.6-25 mg/kg I.V., 50-100 mcg/kg/min (3-6 mg/kg/hr) continuous I.V. infusion rate. May cause some respiratory depression and sedation, and may induce histamine release resulting in peripheral vasodialation. May delay gastric emptying, increase intestinal peristalsis and cause spasm of biliary tract.
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4. Inhalants:

- a. Methoxyflurane: Slowest to change anesthetic level in patient; 45% metabolized.
- b. Isoflurane: Fastest to change anesthetic level in patient; 0.2% metabolized.

5. Miscellaneous injectable restraint agents:

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- c. Etomine 4-8 mg/kg I.V.
- d. Etorphine/Acetylpromazine (Imobilon) .245 mg/10 kg: Diprenorphine (Revivon) .3 mg/kg
- e. Midazolam 100-500 mcg/kg I.M.; Can be combined with propofol (5.g.) and/or fentanyl (6.b.) at a dose of 0.4-0.7 mg/kg/hr as a continuous I.V. infusion for maintenance of anesthesia.
- f. Metomidate 4 mg/kg I.V.
- g. Propofol 0.83-1.66 mg/kg I.V. bolus; 12-20 mg/kg/hr continuous I.V. infusion.
- h. Alflaxalone:
 - i. Induction at 0.47-1mg/kg IV or 1-10 mg/kg IM
 - ii. Maintenance CRI at 0.1-0.3 mg/kg/min +/-xylazine at 0.04ug/kg/min

6. Analgesics:

- a. Fentanyl .02-.05 mg/kg I.M. q2h.
- b. Fentanyl 30-100 mcg/kg/hour I.V. drip.
- c. Sufentanyl 5-10 mcg/kg I.M. q2h.
- d. Sufentanyl 10-30 mcg/kg/hour I.V. drip.
- e. Buprenorphine .005-.02 mg/kg I.M. or I.V. q6-12h.
- f. Butorphanol .1-.3 mg/kg I.M. q 4-6h.
- g. Meperidine 2-10 mg/kg I.M. q4h
- h. Oxymorphone .15 mg/kg I.M. q4h
- i. Pentazocine 1.5-3.0 mg/kg I.M. q4h
- j. Phenylbutazone 10-20 mg/kg P.O. q12h.
- k. Aspirin 10 mg/kg P.O. q4h.

7. Miscellaneous drugs:

- a. Respiratory arrest: (1) Doxapram 1-4 mg/kg I.V. May produce respiratory alkalosis and hyperkalemia. Overdose causes convulsions.
- b. Cardiac arrest:
 - (1) Epinephrine 6-10 .g/kg I.C. or 20-30 .g/kg I.V. (.1-.2 mL/20 kg). Increases heart rate and cardiac output. Causes intense vasoconstriction of renal and splanchnic vasculature. Arrhythmogenic
 - (2) Isoproterenol 1-6 .g/kg I.C. or 2-10 g/kg I.V. Increases heart rate

and cardiac output. Lowers mean arterial blood pressure, requiring concurrent blood volume expansion. Arrhythmogenic.

- c. Antiarrhythmics:
 - (1) Atropine 10-40 g/kg I.V. May cause excessive tachycardia. May predispose to sympathetic-induced arrhythmias.
 - (2) Glycopyrrolate .005-.01 mg/kg I.V. May cause excessive tachycardia.
 - (3) Lidocaine 2-4 mg/kg I.V. 50 mcg/kg/min. continuous I.V. infusion.
 - (4) Bretylium tosylate 3.0-5.0 mg/kg I.V. q30 min.
- d. Bradycardia: (1) Atropine .05 mg/kg I.V.
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Suckow, MA, 1988. The University of Michigan Swine Notes.

Last edited by N. Reyes 12.14.18

Nicholas L. Reyes <nlreyes@uw.edu> From: Sent: Tuesday, August 4, 2020 10:53 AM

To: Michelle Brot; Molly K. Lucas

Subject: Re: Zi-Liu protocol

Attachments: Attachment A-MANUAL OF STANDARD OPERATING PROCEDURES.NR edit

12.14.18.docx

Excellent. I agree that this would be the best way. I have attached the current version of this doc for reference. The only question I have would be in the case that we update the doc (add drugs), is there a way to update it across the protocols which include the procedure without reviewing it for each or would we risk having different versions in different protocols? I don't foresee major changes soon, but we have updated it twice already since it was initially drafted 4-5 years ago.

Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Michelle Brot <mbrot@uw.edu> Sent: Tuesday, August 4, 2020 10:43 AM

To: Molly K. Lucas <mklucas@uw.edu>; Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Molly and Nick,

I agree that as long as it's in there and is consistent with Vet Services' practices, it is simplest to continue with what a lot of groups do, which is a simple procedure called " Vet Services Administered Anesthestics" which refers to an attachment at the end of the procedure that lists all potential anesthetics that may be used in a surgery or other procedure for that species. Here is what it says in Herring's Q2 "Describe step-by-step the procedure for administering the substance(s): " for the anesthetics administration procedure "Veterinary Services will perform all anesthetic administration. Anesthetic agents will be used at their discretion. A list of agents, dosages and routes is appended."

The way Nick described the paramedic protocol with individual entries for each agent sounds like overkill and I'm not sure why that was set up that way.

Thanks! ~Michelle

From: Molly K. Lucas <mklucas@uw.edu> Sent: Tuesday, August 4, 2020 9:54 AM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Michelle can you weigh in on this? I personally don't have an opinion re: how the information is presented as long as it's in there.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Tuesday, August 4, 2020 9:52 AM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Thanks Molly,

The reason I ask is that I met with the paramedic lab group last week and they had a protocol question. In looking at their anesthesia section I saw that they had each drug added in individually (maybe transcribed from the attachment). Seemed like a lot of work to get input and potentially some chance for error in transcribing... that's why I thought I would check before I continue handing it off to investigators.

Nick

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From: Molly K. Lucas <mklucas@uw.edu> Sent: Tuesday, August 4, 2020 9:48:38 AM

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Subject: Re: Zi-Liu protocol

Hi Nick and Michelle,

I know there are plenty of large animal protocols that have the attachment, so unless something has changed in OAW, I think it's fine to do that (there's definitely a precedent).

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To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

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From: Molly K. Lucas <mklucas@uw.edu>
Sent: Saturday, August 1, 2020 3:31:17 PM
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Cc: Nicholas L. Reyes <nlreyes@uw.edu>

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Center for Videoendoscopic Surgery

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To: Molly K. Lucas; Nicholas L. Reyes

Subject: Re: Zi-Liu protocol

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Sent: Tuesday, August 4, 2020 11:36 AM
To: Nicholas L. Reyes; Molly K. Lucas

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It would be great if you could provide this to Zee and ask him to add it to the anesthetic procedure. He is getting much more comfortable in Hoverboard and should be able to modify his current anesthetic procedure to include it. Of course, he knows how to get a hold of me (I think he has my number on speed dial!) if he needs assistance.... ©

Thanks for working with him! ~Michelle

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To: Michelle Brot <mbrot@uw.edu>; Molly K. Lucas <mklucas@uw.edu>

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By the way Michelle, would you still like me to provide this to Zee for his protocol or should I just let him know that you will add this anesthetic plan to the AUP as a new procedure.

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Excellent. I agree that this would be the best way. I have attached the current version of this doc for reference. The only question I have would be in the case that we update the doc (add drugs), is there a way to update it across the protocols which include the procedure without reviewing it for each or would we risk having different versions in different protocols? I don't foresee major changes soon, but we have updated it twice already since it was initially drafted 4-5 years ago.

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Sent: Friday, July 31, 2020 2:48 PM

Subject: Zi-Liu protocol

To: Molly K. Lucas <mklucas@uw.edu>

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To: Molly K. Lucas; Nicholas L. Reyes

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Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

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From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Tuesday, August 4, 2020 9:48:38 AM

To: Nicholas L. Reyes <nlreyes@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Nick and Michelle,

I know there are plenty of large animal protocols that have the attachment, so unless something has changed in OAW, I think it's fine to do that (there's definitely a precedent).

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> Sent: Tuesday, August 4, 2020 9:03 AM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Molly and Michelle,

We did meet virtually with Zee last week and got a much more clear idea of what the anesthetic plan will be. We are putting together a specific initial anesthetic plan for his procedures. I did have a question for you both. In the past for procedures which VS will exclusively be running anesthesia for pigs, the iacuc has accepted our attachment A doc which includes a large range of drug options and allows for some flexibility adjusting anesthetics on the fly. Is this still possible in hoverboard or does each individual drug need to be entered separately? If it all needs to be input individually it probably makes more sense for us to provide Zee with a few options and adjust via protocol modifications if needed (shouldn't be needed too frequently). Thoughts?

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From: Molly K. Lucas <mklucas@uw.edu> **Sent:** Saturday, August 1, 2020 3:31:17 PM **To:** Michelle Brot <mbrot@uw.edu> Cc: Nicholas L. Reyes <nlreyes@uw.edu>

Subject: Re: Zi-Liu protocol

Hi Michelle,

I'm cc'ing Nick so he can let us know if Zee will be making any edits to anesthesia (or anything else) as a result of the meeting.

I was hoping edits could happen prior to it coming back to vet consult, and then hopefully the vet consult will be smoother. I believe it does still need a review (I have not yet looked at it closely).

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From: Michelle Brot <mbrot@uw.edu> Sent: Friday, July 31, 2020 2:48 PM To: Molly K. Lucas <mklucas@uw.edu>

Subject: Zi-Liu protocol

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From: "Molly K. Lucas" <mklucas@uw.edu>

To: "Nicholas L. Reyes" <nlreyes@uw.edu>, Michelle Brot <mbrot@uw.edu>

Sent: 8/4/2020 9:54:57 AM Subject: Re: Zi-Liu protocol

Michelle can you weigh in on this? I personally don't have an opinion re: how the information is presented as long as it's in there.

Molly

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Tuesday, August 4, 2020 9:52 AM

To: Molly K. Lucas <mklucas@uw.edu>; Michelle Brot <mbrot@uw.edu>

Subject: Re: Zi-Liu protocol

Thanks Molly,

The reason I ask is that I met with the paramedic lab group last week and they had a protocol question. In looking at their anesthesia section I saw that they had each drug added in individually (maybe transcribed from the attachment). Seemed like a lot of work to get input and potentially some chance for error in transcribing... that's why I thought I would check before I continue handing it off to investigators.

Nick

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| From: Sent: To: | Michelle Brot <mbrot@uw.edu> Monday, July 20, 2020 1:25 PM Zi-Jun Liu</mbrot@uw.edu> | | |
|---|--|--|--|
| Subject: | Re: Zoom meeting | | |
| Hi Zee, Yes, confirming for 1:30. | | | |
| Thanks, Michelle | | | |
| From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, July 20, 2020 12:07 PM To: Michelle Brot <mbrot@uw.edu> Subject: Zoom meeting</mbrot@uw.edu></zjliu@uw.edu> | | | |
| Hello Michelle, | | | |
| Would you please confirm we will meet via Zoom this afternoon at 1:30? | | | |
| Thank you, | | | |
| Zee | | | |
| Zee Liu is inviting you to a scheduled Zoom meeting. | | | |
| Join Zoom Meeting https://us02web.zoor | m.us/j/ RCW 42.56.420(4) | | |
| Meeting ID: Passcode: | | | |
| | | | |

From: Michelle Brot <mbrot@uw.edu>
Sent: Tuesday, July 21, 2020 10:38 AM

To: Zi-Jun Liu

Subject: Re: Zoom meeting

Sounds good Zee. I will review your changes and provide any feedback I have.

Thanks Michelle

On Jul 21, 2020, at 10:07 AM, Zi-Jun Liu <zjliu@uw.edu> wrote:

Michelle,

I have been feeling much confrontable to work on the HoverBoard after having your very detailed and helpful instructions yesterday afternoon over Zoom. Thank you so much.

I have added all procedures in each Aim including the anesthetic procedures and removed all details in Q5 for each Aim, three figures have been attached as well. I just submitted the revisions. Hopefully, this revision would be OK. I will email Vet Services and request them to review the current anesthetic protocol.

Thank you again,

Zee

From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, July 20, 2020 1:46 PM To: Michelle Brot <mbrot@uw.edu>

Subject: Re: Zoom meeting

Pls sign in again

From: Michelle Brot <mbrot@uw.edu> Sent: Monday, July 20, 2020 1:37 PM

To: Zi-Jun Liu <zjliu@uw.edu> **Subject:** Re: Zoom meeting

Hi Zee,

Not sure what's going on. I didn't see you in the Zoom meeting and then it got ended by the host. Should I try to host one and invite you?

Thanks, Michelle

| From: Michelle Brot <mbrot@uw.edu> Sent: Monday, July 20, 2020 1:24 PM To: Zi-Jun Liu <zjliu@uw.edu> Subject: Re: Zoom meeting</zjliu@uw.edu></mbrot@uw.edu> | | | |
|--|--|--|--|
| Hi Zee, Yes, confirming for 1:30. | | | |
| Thanks, Michelle | | | |
| From: Zi-Jun Liu <zjliu@uw.edu> Sent: Monday, July 20, 2020 12:07 PM To: Michelle Brot <mbrot@uw.edu> Subject: Zoom meeting</mbrot@uw.edu></zjliu@uw.edu> | | | |
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| Join Zoom Meeting https://us02web.zoom.us/j/ RCW 42.56.420(4) | | | |
| Meeting ID: Passcode: | | | |

| Sent: | Monday, July 20, 2020 1:37 PM | |
|---|--|---|
| To: | Zi-Jun Liu | |
| Subject: | Re: Zoom meeting | |
| Hi Zee, | | |
| | going on. I didn't see you in the Zoom meeting and then it got ended by the host. st one and invite you? | |
| Thanks, Michelle | | |
| From: Michelle Brot | t <mbrot@uw.edu></mbrot@uw.edu> | ~ |
| Sent: Monday, July 2 | 20, 2020 1:24 PM | |
| To: Zi-Jun Liu <zjliu@< td=""><td></td><td></td></zjliu@<> | | |
| Subject: Re: Zoom n | neeting | |
| Hi Zee, | | |
| Yes, confirming fo | or 1:30. | |
| Thanks, | | |
| Michelle | | _ |
| From: Zi-Jun Liu <zjl< td=""><td></td><td></td></zjl<> | | |
| To: Michelle Brot <n <b="">Subject: Zoom meet</n> | | |
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| https://us02web.z | :00m.us/ <u>]/</u> | |
| Meeting ID: Passcode: | RCW 42.56.420(4) | |
| | | |

Michelle Brot <mbrot@uw.edu>

From:

From: Michelle Brot <mbrot@uw.edu>
Sent: Sunday, July 19, 2020 7:37 PM

To: Zi-Jun Liu

Subject: Responding to the protocol questions

Hi Zee,

I replaced the Archived Procedures with the updated ones, but I looked over what you had done since we spoke and noticed that you had not made many of the requested changes. I'm not sure if this is because you don't understand what I'm asking for or if you don't know how to do it so you just move on. In either case, we will need to have you make these changes before we can get this protocol approved. Keep in mind that the vets still have to review this and may have additional questions, so you need to be able to make the changes they request.

Below, I have copied and pasted and highlighted the questions that you still need to respond to. I think the best way to do this is to have a Zoom session where you show me your Hoverboard screen and I can try to talk you through the questions and help you to work on the responses. This is taking quite a bit of my time and I have many other protocols to work on so I would like you to spend some time reviewing the questions below that you didn't address appropriately. So we can be most efficient, be prepared to know what I am asking in the questions so you're ready to answer them.

Please set up a time and provide a Zoom link and I will work with you to get this done. I am flexible tomorrow (Monday) but would prefer an afternoon time so I can get some of my other work done in the morning. Tuesday is an option as well.

Regards, Michelle

- 1) "In Exp 002, Q5, in the second paragraph you refer to "coblation." I'm not familiar with what that is but it appears to be a procedure (Survival Surgery?) so you need to make a procedure for it and put all the details that you have about it in Q5 into the procedure."
- 2) "In a previous question about your Aim 2 experiment, I asked about coblation and you responded "This is widely used surgical approach to reduce the volume of the tongue base or tongue body, also called SMILE Submucosal minimally invasive lingual excision."

Thanks for this explanation. As I had mentioned in my question, you will need to create a procedure for this Survival Surgery and remove the details from Q5."

- 3) "The Special Diet you have included in Aims 1 and 2 is a High Fat diet that will be provided continuously for the pigs in your studies. If that is the case, you need to mention that in Q5. I think you are planning to withhold that High Fat diet on recording days and only feed the pigs the Barium diet then? Please make that clear in Q5. "
- 4) "Also, as I had previously requested, please create a Special Diet procedure for this: "(After 10-15¹ of feeding on barium sulfate Opti-Bar mixed solid, pasty, and liquid diets,..."
- 5) "Please finish filling out the information in the Special Diet procedure you have now for the High Fat diet. Right now, there are no responses to Q5 and Q6 in that procedure."

6) "In Aim 2, Q5, the last section says that all tracking and terminal procedures will be the same as for Aim 1. However, in your list of procedures, you have Perfusion, which isn't in Aim 1, since you plan to euthanize those pigs with Pentobarbital, correct?"

There is still a Non-Survival Surgery: Perfusion procedure in Aim 2.

7) "Also, the timeline needs to be fleshed out for Aim 2. Will there be recordings at week 1, 3, and 5 after coblation surgery?"

This section below still needs to have the information since you responded that there be recordings at week 1, 3, and 5 after coblation surgery.

Day 28 and thereafter: Longitudinal tracking and terminal procedures:

All longitudinal tracking and terminal procedures same as in Experiment 1.

- 8) Aims 1 and 2: "Days 1-7: Pig¹s training and acclimation, focus on feeding training with wearing pig¹s jacket." New question: Please be more specific about how you will do the training for feeding and how long the pigs will wear their jacket.
- 9) "In a previous question, I said "In Exp 001, Q5, it says "Crystals #1 and #2 will be implanted 2mm posterior to the two circumvallate papillae (boundary of the tongue base and body) and 3mm"
- 1) It looks like this sentence needs to be finished.
- 2) Please create an Implant procedure for the crystals
- 3) Please create a Survival Surgery procedure for implanting the crystals and remove most of these details from Q5 since they should be added to the procedure instead."

Your response that this is the same procedure as in another protocol. The protocol you referred to is closed and we don't refer to other protocols to explain how procedures are done. Each protocol has to stand on its own, as does each experiment within a protocol. Please create the procedures as requested and remove the details of those procedures from Q5."

10) "I'm not sure why your Aim 2 experiment includes a Non-Survival surgery that seems to contain many of the elements of the survival surgery that is described in Aim 1 (and may be relevant for Aim 2). Please review this and see if you can convert some of this to a Survival Surgery or explain in Q5 if you are planning a Non-Survival Surgery as part of this experiment.

Your response was "I don't think a non-survival surgery are included in both Aims. All proposed surgeries are

survival ones." But, it doesn't look like you have created the Survival Surgeries you need and you still have the Non-Survival surgeries as procedures in both Aims that you don't need.

11) Also, as you are going through this procedure, please remove the information that states "In this terminal procedure, the animal will be sedated and anesthetized on the 6th floor and then transported to the lab." as it looks like you are going to be exclusively in Brotman and ARCF."

It doesn't look like you removed this information about the location of the terminal procedure, as I

requested.

From: Michelle Brot <mbrot@uw.edu>
Sent: Monday, August 31, 2020 2:18 PM

To: Zi-Jun Liu

Subject: Still need some questions answered.....

Hi Zee,

The IACUC reviewer wanted me to check with you on a couple items:

1) Are the obese pigs in Aim 2 going to be fed a high fat diet while they are at UW? If so, the Special Diet procedure that you created needs to be added back into the list of procedures and this needs to be mentioned in Q5 of Exp 002. If not, the second sentence in the Q12 Husbandry exceptions for the Special/medicated Diet needs to be removed:

Pigs - Barium diet will be provided during each recording session. Ad lib feeding Special/medicated diet will be applied for obese minipigs with a high fat diet.

- 2) In Aim 01, Q5, it says "Day 48: Terminal recording. *Please note that the terminal surgery may be done at an earlier timepoint if the instrumentation fails and has to be reimplanted as part of the terminal surgery.*" and there is the same sentence in Aim 2 for Day 57.
- a) Is the "terminal surgery" the same as the "Stimulation Surgery"? You need to refer to it in Q5 as you call it in the Procedure Name.
- b) When I read about the Terminal Recording procedure in "Behavioral Testing: Terminal Recording (w/Food Restriction)", it says that Terminal Recording is the same as Longitudinal Tracking (see Longitudinal Tracking). But there is no Longitudinal Tracking procedure. If it is the same as the Longitudinal Tracking, why aren't you just using that procedure?
- c) It also says "After terminal recording, the stimulation session will be performed (See Stimulation)." This final Non-Survival surgery should be part of the timeline in Q5 of the experiment. We need to know when this is happening. Is this the day after the Terminal recording? Does that mean the pig may be fasted two days in a row?
- 3) Within the Stimulation surgery, it says "3D deformational changes in the tongue base (SONO) and respiratory parameters (Pneumotach system) will be recorded along with stimulation pulses under x-ray videofluoroscopy." Is that in addition to the same procedures occurring just prior as part of the Terminal Recording procedure?

If you need clarification on these questions, you can call me (206-291-3058).

Regards, Michelle From: Michelle Brot <mbrot@uw.edu>
Sent: Thursday, August 20, 2020 7:30 PM

To: Zi-Jun Liu

Subject: Timeline estimate

Hi Zee,

I have moved your protocol into Committee Review so it should be approved a week from tomorrow (Aug. 28) as long as the Commitee doesn't have any questions.

However, in the meantime, the vet requested that you place some parameters around this general statement you put in that adds flexibility: "Please note that the following timelines are approximate, and subject to be modified upon the detailed situation." This is for the general timeline in Q5 for each experiment. Would you be able to tell me about how long you think the dates could vary, e.g., the timeline could vary "up to x days". I can add the information for you.

Thanks, Michelle From: Molly K. Lucas <mklucas@uw.edu>
Sent: Sunday, August 16, 2020 1:35 PM

To: Michelle Brot

Subject: Zee Liu pig protocol

Hi Michelle,

I just turned around my 2nd vet consult. One thing I didn't put in Hoverboard but wanted to ask you to think about, is that in response to my recommendation to add some flexibility in timing in Q #5 of the experiments, he added, "Please note that the following timelines are approximate, and subject to be modified upon the detailed situation." I think this is an improvement, because sometimes things happen like the MRI isn't available, or a fasting mistake is made, and procedures have to be put off a day or two. I am thinking that there are often more specific parameters around this, though, esp in large animal protocols (e.g., I've seen some that say the timeline could vary but "up to x days").

Might be a good topic to check in with the other reviewers on to see what they think/how they've been approaching this type of thing.

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Thanks, Molly From: "Molly K. Lucas" <mklucas@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/12/2020 4:48:53 PM

Subject: Zee Liu protocol - revision

Hi Nick,

The revision is back in my inbox. So far I've read the responses to my questions, which overall look promising (e.g., no re-implantation except at terminal surgery). I still need to go through and verify that all of the changes were made and with sufficient detail, etc. but so far, so good.

Here's the link if you have time to have a look:

https://hoverboard.washington.edu/Hoverboard/sd/Rooms/DisplayPages/LayoutInitial?container=com.webridge.entity.Entity%5BOID%5BBBD9E52211666B4AB9BA57EE24AED8CC%5D%5D&tab2=6AFC50FC61973849A9BA4623A8F4A280

Here is the response about the red rubber catheter. I guess the follow up question may be how long it stays in/how it is removed, if it is left in for a recording session (meaning they've recovered from anesthesia)... I'm not sure if that info is in there somewhere or not...

Thanks, Molly

Veterinarian Change Request (response required)
Jump To: Experiments
Liu-Minipig: Baseline recording:

- -Re: "After 10-15' of feeding on the barium diet, sensors and wire electrodes will be removed, and the pig will return to its pen." Is this 10-15 minutes? Please edit to clarify.
- -Please edit to include the purpose of the red rubber catheter and to remove the size (#10), as you may need different sizes for different size pigs.
- -I'm not sure I understand the part about replacing the mask with the red rubber catheter. Vet services is under the impression that inhalant anesthesia (e.g., isoflurane) delivered by mask can be used for all of the imaging procedures. Is this correct?

Change Request Completed - Zi-Jun Liu - 8/10/2020 10:31 AM Red rubber catheter is for recording the respiratory parameters via BioRadio system during feeding. Size #10 has been removed.

From: Molly K. Lucas <mklucas@uw.edu>
Sent: Wednesday, August 12, 2020 4:49 PM

To: Nicholas L. Reyes

Subject: Zee Liu protocol - revision

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| From: | Molly K. Lucas <mklucas@uw.edu></mklucas@uw.edu> |
|---------------------------------|---|
| Sent: To: | Wednesday, August 5, 2020 3:47 PM Nicholas L. Reyes |
| Cc: | Michelle Brot |
| Subject: | Zee protocol Q |
| Hi Nick, | |
| I'm doing the vet co | onsult now and just wanted to double check a few things with you. |
| looks OK as everyo entry for | twice re: the personnel assigned to surgery and anesthesia. I think the surgery list ne on it appears to be certified (although Michelle, I don't actually see a certification just that Part 1B and Part 2 were waived? Everyone else listed for surgery has you check in that please?). |
| However, the anest | thesia personnel are pasted below. I am thinking it should only be vet services listed, rrect to you? |
| Molly | |
| | FERPA |
| | RCW 42.56.070(1) |
| NIRANJAN BALU | |
| Sue Herring | |
| Daniel F Leotta | |
| Zi-Jun Liu | |
| Katherine Rafferty | |
| Vet Services | |
| Jeffrey Thiel | |
| [X] | |

[X]

| From: "Molly K. Lucas" <mklucas@uw.edu> To: "Nicholas L. Reyes" <nlreyes@uw.edu> CC: Michelle Brot <mbrot@uw.edu> Sent: 8/5/2020 3:47:05 PM Subject: Zee protocol Q</mbrot@uw.edu></nlreyes@uw.edu></mklucas@uw.edu> | | |
|--|---|--|
| Hi Nick, | | |
| I'm doing the vet consult now a | nd just wanted to double check a few things with you. | |
| looks OK as everyone on it appe | e personnel assigned to surgery and anesthesia. I think the surgery list ears to be certified (although Michelle, I don't actually see a certification that Part 1B and Part 2 were waived? Everyone else listed for surgery ck in that please?). | |
| However, the anesthesia person listed, does that sound correct to | nnel are pasted below. I am thinking it should only be vet services to you? | |
| Molly | | |
| | FERPA | |
| NIRANJAN BALU | RCW 42.56.070(1) | |
| Sue Herring | | |
| Daniel F Leotta | | |
| Zi-Jun Liu | | |
| Katherine Rafferty | | |
| Vet Services | | |
| Jeffrey Thiel | | |
| | | |
| | | |

| From: Sent: | Molly K. Lucas <mklucas@uw.edu> Wednesday, August 5, 2020 3:47 PM</mklucas@uw.edu> |
|---|---|
| To: | Nicholas L. Reyes |
| Cc: | Michelle Brot |
| Subject: | Zee protocol Q |
| Hi Nick, | |
| I'm doing the vet con | sult now and just wanted to double check a few things with you. |
| looks OK as everyone entry for | vice re: the personnel assigned to surgery and anesthesia. I think the surgery list on it appears to be certified (although Michelle, I don't actually see a certification just that Part 1B and Part 2 were waived? Everyone else listed for surgery has u check in that please?). |
| However, the anesthodoes that sound corre | esia personnel are pasted below. I am thinking it should only be vet services listed, ect to you? |
| Molly | |
| | FERPA |
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| NIRANJAN BALU | |
| Sue Herring | |
| Daniel F Leotta | |
| Zi-Jun Liu | |
| Katherine Rafferty | |
| Vet Services | |
| Jeffrey Thiel | |
| [X] | |

[X]

From: Michelle Brot <mbrot@uw.edu>
Sent: Friday, July 31, 2020 2:49 PM

To: Molly K. Lucas Subject: Zi-Liu protocol

Hi Molly,

I see that you're out of the office today. I just wanted to check in with you to see if you will need me to send Zee's protocol to Vet Consult again for you to review it since it's currently in Pre-Review. I don't see any indication that changes were made after their Vet Services meeting about the anesthesia plan yesterday so I'm just touching base in case you have any more information. Hope you are enjoying your time away and we can connect next week.

Take care, Michelle From: Michelle Brot <mbrot@uw.edu>
Sent: Friday, July 31, 2020 2:49 PM

To: Molly K. Lucas Subject: Zi-Liu protocol

Hi Molly,

I see that you're out of the office today. I just wanted to check in with you to see if you will need me to send Zee's protocol to Vet Consult again for you to review it since it's currently in Pre-Review. I don't see any indication that changes were made after their Vet Services meeting about the anesthesia plan yesterday so I'm just touching base in case you have any more information. Hope you are enjoying your time away and we can connect next week.

Take care, Michelle Exp 1 and 2, Q #6: It looks like a new Euthanasia procedure was made and replaced the previous one which I had edited. Like the previous version I reviewed, it lists phenobarbital, but it is pentobarbital solution that is used for euthanasia. I deleted the new Team procedure from both Experiments and replaced it with the Standard procedure. The Standard is "pre-approved" by the IACUC and reflects what vet services does, so I strongly recommend using this version unless there is a specific reason not to.

No action necessary on your part if you are amenable to this change, otherwise further edit as needed.

Other: Liu-Minipig: Catheter and Wire Electrode (Team) and Other: Liu-Minipig: Baseline recording, ver. 1 (Team):

-Please edit to provide more detail re: how the red rubber catheter that has been sutured in will be removed (I'm not sure exactly where the sutures might be placed and whether re-sedation/anesthesia will be needed for removal?).

Substance Administration: Liu-Minipig: Post-op analgesic plan, ver. 1 (Team): Currently the only substance entry for carprofen is for the IV route. Please edit to create separates SC and PO (oral) substance entries in addition to the IV entry. Generally oral administration is preferred/attempted post-operatively (since it is the least invasive). It's helpful to have all of the options, and injectable is generally used at the time of surgery when animals are anesthetized.

Survival Surgery: Liu-Minipig: Tongue base reduction surgery, ver. 1 (Team)

And

Survival Surgery: Liu-Minipig: Implantation (Team)

Q 4i: fyi, I edited the text that states, "For pain relief and infection control, Fentanyl patch (for dose say that vet services will determine correct patch size/dose) and the Carprofen, which is an NSAID (2-4 mg/kg IV or SC every 24 hr or 2 mg/kg PO every 12 hr) will be applied."

I replaced it with, "For pain relief and infection control, pigs will be given an opioid for a minimum of 72 hr (either a Fentanyl patch, SR buprenorphine, or regular buprenorphine) and the NSAID Carprofen for a minimum of 72 hr."

And in Q #6 I changed "will" to "may" as vet services may not recommend ointment: "Certain antibiotic ointments will be administered per Vet Services' recommendation."

No action necessary on your part if you are amenable to these edits, otherwise further edit as needed.

Substance Administration: Liu-Minipig: Excede (ceftiofur) injection (Team): I made some minor edits, e.g., to indicate that it will be pharm-grade, to include the concentration, and to remove the volume (since it's only required for rodents and intracranial injections). No action necessary on your part if you're amenable to these edits, otherwise further edit as needed.

Non-Survival Surgery: Liu-Minipig: Stimulation (Team):

For the question, "Describe how the animal, surgeon, and instruments will be prepared for surgery:" Please edit to replace the current response ("There will be the same preparation for the animal, surgeon, and instrument as for the terminal recording.") with a response that addresses animal prep (skin cleaning/hair removal if necessary) of the surgical site as well as whether sterile vs. clean (but not necessarily sterile) instruments, gloves, etc. will be used, and what the surgeon will wear. The terminal recording procedure currently does not address prep of the animal, surgeon, or instruments and the terminal surgery procedure is the best place for this information.

From: Leandra Mosca <mosca@uw.edu>
To: "Nicholas L. Reyes" <nlreyes@uw.edu>

Sent: 8/10/2020 12:21:15 PM

Subject: Zoom Link RE: Liu Pig Anesthesia

Leandra Mosca is inviting you to a scheduled Zoom meeting.

Topic: Liu Anesthesia

Time: Aug 10, 2020 01:00 PM Pacific Time (US and Canada)

Join Zoom Meeting

https://washington.zoom.us/j/

RCW 42.56.420(4)

Meeting ID:

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- +1 669 219 2599 US (San Jose)
- +1 669 900 6833 US (San Jose)
- +1 720 928 9299 US (Denver)
- +1 971 247 1195 US (Portland)
- +1 470 381 2552 US (Atlanta)
- +1 646 518 9805 US (New York)
- +1 646 876 9923 US (New York)
- +1 651 372 8299 US (St. Paul)
- +1 786 635 1003 US (Miami)
- +1 267 831 0333 US (Philadelphia)
- +1 301 715 8592 US (Germantown)
- +1 312 626 6799 US (Chicago)
- +1 470 250 9358 US (Atlanta)

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162.255.36.11 (US East)

221.122.88.195 (China)

115.114.131.7 (India Mumbai)

115.114.115.7 (India Hyderabad) 213.19.144.110 (EMEA) 103.122.166.55 (Australia) 209.9.211.110 (Hong Kong SAR) 64.211.144.160 (Brazil) 69.174.57.160 (Canada) 207.226.132.110 (Japan) Meeting ID:

RCW 42.56.420(4)

From: Nicholas L. Reyes <nlreyes@uw.edu> **Sent:** Friday, August 7, 2020 10:18 AM **To:** Leandra Mosca <lmosca@uw.edu>

Subject: Re: Liu Pig Anesthesia

No problem. Like I said there is no major urgency on this... Just good to discuss it while its fresh in everyone's head. See you Monday at 1pm Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle nlreyes@uw.edu 206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Friday, August 7, 2020 10:15 AM To: Nicholas L. Reyes lmosca@uw.edu >

Subject: Re: Liu Pig Anesthesia

Hey Nick, 1pm on Monday works. Thank you so much and I really apologize. Someone still needed to sign off on Megan teaching Sx 1A.

Leandra

On Aug 7, 2020, at 9:11 AM, Nicholas L. Reyes <nlreyes@uw.edu> wrote:

I have a few meetings this afternoon starting at 1pm so might not give us enough time. Wanna push until Monday? I could make 1pm on Monday work.

Nick

Nicholas Reyes DVM, MS, DACLAM Sr. Staff Veterinarian Co-Director of Animal Facility Operations Dept. of Comparative Medicine University of Washington, Seattle

nlreyes@uw.edu 206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Friday, August 7, 2020 8:36 AM To: Nicholas L. Reyes < lmosca@uw.edu >

Subject: RE: Liu Pig Anesthesia

Hi Nick,

Would it be possible to bump our meeting back to 12:40p? I had to switch into an AUTS class today that goes until 12:30p.

Thanks, Leandra

From: Nicholas L. Reyes < nlreyes@uw.edu>
Sent: Thursday, August 6, 2020 11:39 AM
To: Leandra Mosca < lmosca@uw.edu>

Subject: Re: Liu Pig Anesthesia

How about noon. That work?

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

nlreyes@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu
Sent: Thursday, August 6, 2020 11:26 AM
To: Nicholas L. Reyes < lmosca@uw.edu>

Subject: RE: Liu Pig Anesthesia

Hi Nick,

Thanks! I am available any time tomorrow. Mid-morning to afternoon would be ideal (if possible) since I'm doing some cell work in the morning- but I can definitely work with your schedule

Thank you, Leandra

From: Nicholas L. Reyes nlreyes@uw.edu Sent: Thursday, August 6, 2020 8:12 AM To: Leandra Mosca lmosca@uw.edu >

Subject: Re: Liu Pig Anesthesia

Hey Leandra,

Great job. Let's definitely get together to discuss. I have a couple suggestions based on previous experience with similar experiments. When would be a good day/time to zoom. FYI I did send Zee the attachment doc which outlines our many porcine drug options. Not sure if you've seen this doc already but its somewhat of an overkill formulary that IACUC approves for pig procedures wherein VS will run all anesthesia. By approving the blanket formulary it lets us adjust on the fly (I attached it here for your reference). The doc that you are working on will be for our internal use so we have a little time to finalize it. Let me know when you can meet.

Thanks, Nick

Nicholas Reyes DVM, MS, DACLAM

Sr. Staff Veterinarian

Co-Director of Animal Facility Operations

Dept. of Comparative Medicine

University of Washington, Seattle

nlreyes@uw.edu

206-543-0267

From: Leandra Mosca < lmosca@uw.edu Sent: Wednesday, August 5, 2020 3:14 PM To: Nicholas L. Reyes < nicholas L. Reyes < <a href="mailto:nicholas"

Subject: Liu Pig Anesthesia

Hi Nick,

I have attached my summary/recommendations for the Liu pig project.

The pigs do not need sedation or restraint for removing equipment after recording—I confirmed

with Zee.

Should we discuss this when you are available?

Thanks, Leandra

Leandra Mosca, DVM
Laboratory Animal Medicine Resident
Department of Comparative Medicine
University of Washington
LMosca@uw.edu
206-616-7772